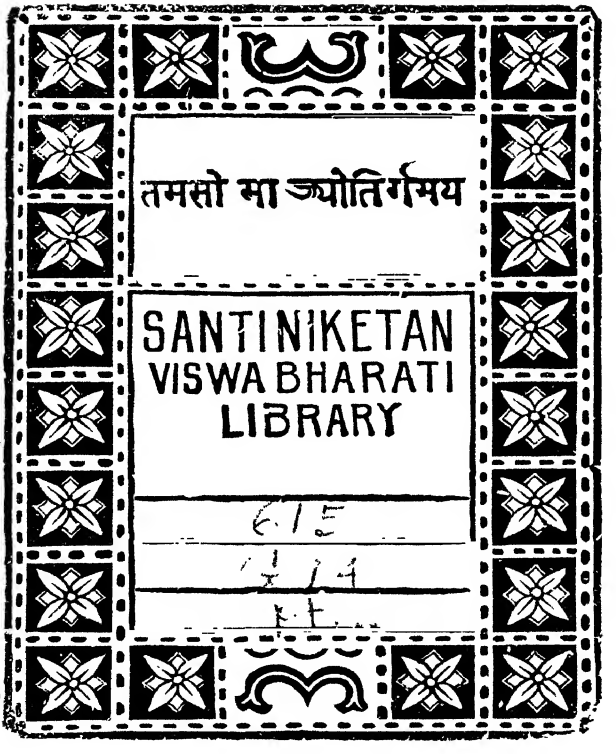
तमसो मा ज्योतिर्गमय
SANTINIKETAN
VISWA BHARATI
LIBRARY
615

Recent Advances

IN

Therapeutics

PART II

By

J. R. GOYAL. M.B.B.S.

◆

Publishers:

The Manager **The MEDICAL NEWS**

P. O. BOX 81 - - - - - DELHI.

1st Edition **1941** ***Price Rs. 3/8***

PREFACE

Some epoch making discoveries have been made in medicine during the last few years Sulphonamide group of drugs is one and has been dealt with fully in the first part.

Vitamins, Hormones, Liver Extract, Protamine zinc insulin, Intravenous anaesthesia, closed plaster method of treatment of wounds and fractures, the New antacids, New antisyphilitic drugs and others are notable contributions to the art of medical treatment and have been dealt with in this volume. It is hoped that the book will prove useful to the general practitioner and the student alike.

The author is sorry for few printing mistakes for which an "Errata" has been added at the end "Errata" may be consulted during the study of the book.

1 8 41
Mission Church Road

J. R. Goyal.

TABLE OF CONTENTS.

CHAPTER I.

Vitamins.

Vitamin deficiency. Now a days gross vitamin deficiency diseases such as rickets, scurvy, beriberi, pellagra or Xeropthalmia are rare. But the so called "minor" deficiencies are common and often un-detected and so the maladies, and the loss of health, vigour and full function which they cause are of great importance.

Causes of deficiency.

(1) Dietary supply of vitamins may be insufficient because of poverty, prejudice, climate, lack of appetite or the use of unbalanced diet in the treatment of such conditions as:—

(2) Typhoid fever, Bright's disease, peptic ulcer, etc.

(3) There may be failure on the part of the body to synthesise as the vitamin D due to absence of sunshine or vitamin K through lack of formative bacterial action in the intestine.

(4.) The vitamin content of the diet may be such that it would have been adequate under

ordinary circumstances, but its absorption from the digestive tract may be diminished by chronic gastro-enteritis, pyloric stenosis, achlorhydria, vomiting, biliary obstruction etc.

(5) Vitamin requirements have been increased by the extra calls of pregnancy, lactation or rapid growth.

(6) There may be partial failure to utilise the vitamins due to some intercurrent disease as diabetes or cirrhosis of liver.

Role of Vitamin A.

Vitamin A exerts its influence particularly on the eye and the epithelium. It is essential for the growth and development of the young. When experimental animals are deprived of Vitamin A the two earliest effects to be observed are cessation of growtn and ulceration of the cornea. As the avitaminosis progresses patchy dryness, areas of thickened epithelium, loss of lustre and wrinkling of the conjunctiva occurs. There is also decreased secretion of tears. Keratomalacia is the last stage of the eye manifestations.

Skin changes are also early indications of the disease of vitamin A deficiency. Dryness of the skin is

preceeded by the eye changes by several weeks. The skin under-goes more marked and extensive changes than any other tissue excepting the eyes. Keratoctic papules of varying size appear distributed over the extremities and shoulders. Vitamin A has influence on tooth development as well. Enamel and dentin formation are dependent upon an adequate supply of vitamin A. In experimental rats the deficiency of A gave rise to formation of urinary calculi consisting of calcium carbonate.

It has an effect on ovarian function as well. In human beings especially children its deficiency causes xeropthalmia and keratomalacia. Phrynoderma or toad skin is common and is associated with angular stomatitis. It causes night blindness also. There is defect in adaptation of eyes rapidly and efficiently to dim light.

Vitamin A deficiency may be a factor in causing myopia as well. The food of the Japaneese indicates a deficiency of vitamin A. So they have a large national problem in the poor eye sight of their young men and are very much inclined to myopia.

Experiments on rats have shown that a diet deficient in Vitamin A and fat tends to give rise to defects in scleral development. Deficiency of

Vitamin A during the period of growth weakens the cornea and sclera which subsquently gives rise to myopia and myopic astigmatism.

The daily requirements of carotene varies between 43 and 103 units per kilogram of body weight.

Vitamin A is fat soluble and is found in the liver oils of fish. It is found in great abundance in the vegetable oil.—the redpalm oil. In vegetables such as carrots and tomatoes its precursor carotene which is fat soluble is found which becomes changed in the body of man or animals into Vitamin A. Carotene was first isolated from carrots hence the name carotene and is found in abundance in the pigment of outer coat of carrots.

Therapeutic Uses.

(1) *Night-blindness or nyctalopia.* If this is due to the deficiency of Vitamin A it is cured by giving Vitamin A or carotene. Cases of nyctalopia exist which do not respond to treatment with Vitamin A. These cases are not due to vitamin deficiency.

(2) X eropthalmia is cured by internal administration of Vitamin A. Opthalmic conditions and injures to eyes by gas are cured by local application of Vitamin A.

(3) *Skin Diseases.* Vitamin A has been found of value in treating dry and scaly skin and papular eruptions, malignant ulcers and other skin lesions.

(4) Dental troubles as caries and pyorrhoea may also be prevented by its use.

(5) Administration of Vitamin A has given good result in hypoacidity.

(6) There are too much claims about Vitamin A in increasing the resistance of the body to infections and in promoting growth. A well balanced diet is always preferable in such cases rather than a costly treatment with Vitamin A. Vitamin A may have some effect in warding off respiratory troubles as it has a selective action on epithelium. Statements conveying the impression that Vitamin A is more important in promoting growth than other food essentials are misleading and objectionable.

(7) There is no evidence to warrant the claim that the ingestion of sufficient Vitamin A will prevent the formation of renal calculi in man.

A well-balanced diet should contain a daily minimum of 3 000 international Units.

Some common sources of Vitamin A.

100 grams of each of the following will contain .....international units of Vitamin A.

(1)	Halibut Liver oil	3,000,000—15,000,000
(2)	Cod Liver oil	50,000—200,000
(3)	Butter	2000—3000
(4)	Red palm oil	59,000—200,000
(5)	Shark Liver oil	about cod liver oil or more
(6)	Amaranth	2500—11000
(7)	Cabbage	2000
(8)	Celery	5760—7470
(9)	Coriander	10360—12630
(10)	Curry leaves	12600
(11)	Drumstick	11,380
(12)	Gram leaves	6700
(13)	Mint	2700
(14)	Spinach	2630—3500
(15)	Carrots	2020—4300

The Vitamin B. Complex

The term Vitamin B Complex is applied to a group of substances which have been shown to be constituents of what was formerly called vitamin B. It consists of :—

(1) Vitamin B_1 the anti beriberi Vitamin which prevents beriberi in man and poly neuritis in animals.

(2) Riboflavin, a Compound necessary for growth

in chicks and rats, and for the prevention of cataract in rats. It is a component of an oxidation-reduction system of living cells.

(3) Nicotinic Acid (amide), recently reported to be curative of black tongue in dogs.

(4) P-P. Factor, a factor for the prevention of human pellagra.

(5) Filtrate Factor, a factor for the prevention of a nutritional dermatosis in Chicks.

(6) Vitamin, B_3, a factor necessary for rapid gains in weight and normal nutrition of pigeons.

(7) Vitamin B_4, a factor for the prevention of a specific paralysis in rats and chicks.

(8) Vitamin B_5, a factor necessary for weight maintenance of pigeons.

(9) Vitamin B_6, or vitamin H, a factor for the prevention of a nutritional dermatosis in rats.

(10) Factor W, a factor necessary for growth of rats.

Only B_1, pellagra preventure factor, Nicotinic acid, riboflavin, vitamin B_6 and 'filtrate factor' have thus far been definitely shown to be necessary in human nutrition and to be of therapeutic value in

human disease.

Vitamin B_1

This vitamin is recognized as being of fundamental importance in connection with the disease beriberi. The naturally occurring substance is known as "Thiamin" and " Thiamin chloride" as the hydrochloride of the vitamin. It is now being manufactured synthetically. It is the only known naturally occurring compound containing the thiazole nucleus. It is the only known Vitamin containing sulphur. It is water soluble. Little destruction of B_1 occurs in foodstuffs exposed to 100°C, but undue heat is undesireable and, as the vitamin is sensitive to alkalies, the addition of cooking soda to vegetables should be avoided. It is to some extent adsorbed on the starches, but it may be lost by solution in cooking ; therefor cooking water and juices should not be discarded but should be incorporated in to soups, sauces or gravies.

The average daily requirement for man is about 1—2 mg. This vitamin B_1 is not only related in some specific way to the function of the nervous system but it plays an equally important part in the nutrition of organisms which do not posess a nervous system ;

thus certain fungi which fail entirely to grow on a medium consisting of carbohydrates and mineral salts, will grow vigorously when small amounts of vitamin B_1 have been added. The addition of other substances however fail to make the medium capable of supporting the growth of the fungus.

As there is obviously a direct relation between the rate of cell metabolism and the basal metabolism rate B. M. R., it follows that other conditions being equal, the minimum amount of vitamin B_1 required by the body will be determined by the B. M. R. Anything which tends to raise the B. M. R. will also increase the requirements of the body for vitamin B_1. Thus rats kept on a standard diet containing adequate amounts of vitamin B_1 will show evidence of vitamin B_1 deficiency when the B. M. R. is raised by the administration of thyroxine Increased metabolism as a cause of vitamin B_1 deficiency is of considerable practical importance, prolonged fever, pregnancy, lactation, rapid growth, may each precipitate clinical mani-festations of deficiency when the intake of vitamin B_1 is only just adequate for the minimum ordinary requirements. Vitamin B_1 deficiency may result from diminished intake as faulty diet, alcoholism, food fads, poverty or vomiting ; it may

also result from diminished absorption in achlor hydria, carcinoma ventriculi, diarrhoeas, coeliac disease, ulcerative colitis, dysentery etc. It may also result from increased demands due to pregnancy, lactation, prolonged fever. Major forms of deficiency result in polyneuritis. The clinical features are like other forms of poly-neuritis. Muscle tenderness, painfull para-esthesias and symmeterical "glove and stocking" sensary loss as well as weakness of the limbs are present. During the early stages of the disease neuritis of a single peripheral nerve (e.g.ulnar) or loss of tendon jerks may be the only clinical manifestation. Other manifestations of vitamin B_1 deficiency are oedema, tachycardia, or heart failure with congestion, symmeterical erythematous desquamating dermatitis, glossitis, stomatitis or diarrhoea

Minor deficiency. Minor deficiency is much more common and is often over looked. The vitamin B_1 is essential to growth and development of the young. It has a pronounced effect on the digestive system, assists in maintenance of normal weight and mental acuity and the normal function of the cardio-vascular system. Minor deficiency causes anorexia, loss of weight, mental and cardio-vascular

disturbances.

Six patients were kepr for 88 days on a diet deficient in vitamin B_1. The more active subjects were the first to experience symptoms. These were depressed mental states, generalised weakness, dizziness, backache, soreness of muscles; palpitation, dyspnea and precordial distress on exertion, insomnia, anorexia, nausea, vomiting, loss of weight, atony of muscles, slight roughness of the skin, faint heart sounds, lowered blood pressure and bradycardia when at rest with tachycardia and sinus arrhythmia on exertion. In all cases physical activity greatly decreased. There were also seen states of apathy, reawakening of psychotic trends, difficulty of thought and memory, photo-phobia, headache abdominal distention, sensations of cold and heat, burning of the soles of the feet, numbness of the legs, fatigue of ocular muscles, tenderness of the muscles of the calves and depressed tendon reflexes.

Changes in the heart, and oedema were not seen. Anaemia did not develop and there was no redenning of the skin or of the tongue. Capacity for work fell progressively.

Degree of debility induced was impressive. It resembled in early stages neurasthenia and anorexia

nervosa in later stages. Symptoms of the beri beri as oedema, cardiac dilatation and peripheral pain were absent. So in all cases of neurasthenia, deficiency of vitamin B_1 should be kept in mind.

Therapeutic Uses:—

(1) Vitamin B_1 is of value in correcting and preventing beri beri.

(2) Vitamin B_1 is of value in cases of poly neuritis. In such cases oral method is not sufficient. 20—50 mgm daily of vitamin B_1 is given intravenously for 1—2 weeks.

(3) Oedema, ascites, congestive heart failure Vitamin B_1 by intravenous or hypodermic injection causes diuresis. It has no diuretic action in the absence of pathological states.

(4) Vitamin B_1 is of value in correcting and preventing anorexia of dietary origin in certain cases.

(5) Vitamin B_1 is of value in securing optimal growth of infants and children.

(6) Nervous disorders.

i *Parkinsonism.* N. Holmin treated 12 cases, 2 improved, 3 somewhat favourably influenced, and 7 showed no im-

provement. The improvement consisted in changes of the speech, better articulation, disappearance of the greasiness of the face, and decrease of tremor and rigidity.

ii 2 cases of neuritis were improved considerably.

iii Of 3 cases of disseminated sclerosis, 2 improved with decrease of tremor and spasm and disappearance of constipation.

iv One case of spastic paraplegia, after 3½ months of vitamin B_1 treatment showed return of motility and disappearances of headaches. In above cases 20 mg. of B_1 were injected intramuscularly daily.

v Pain of ischaemic origin. M. Naide treated 10 cases with 100 mg. of vitamin B_1 intravenously. Seven were completely relieved, 2 partially relieved and one obtained no relief from pain.

vi Vitamin B_1 has proved useful in neuralgia and neuritis of leprosy, in intractable neurotic vasodilatory symptoms in the hands and feet associated with severe

pain and paraesthesia.

vii Vitamin B_1 may be useful in the treatment of optic neuritis and toxic ambylopia.

viii *Neuralgia.* Sometime large doses of vitamin B_1 have given good results in trigeminal neuralgia, intercostal neuralgia and sciatica. Bohm treated two cases of trigeminal neuralgia with injections of crystalline vitamin B_1 with complete success. Hofer Von Lohensteen tried B_1 in one case each of neuralgia of trigeminal, occipital and intercostal nerves, and in two cases of Sciatica. He gave 6—10 intramuscular injections with satisfactory results in all. I. Buksh treated seven cases of trigeminal neuralgia with vitamin B_1 therapy and with the exception of one all have been greatly benefitted by this treatment.

Vitamin B_1

Role of Vitanin B_1 in Delirium Tremens.

Hugh E. Kiene, Robert J. Streitwieser and Himon Miller contend that the cause of delirium tremens is essentially a vitamin B_1 deficiency which has been

brought on by sudden deficits in the maintenance requirements. Inadequate, irregular and at times total abstinence of diet is practically universal in acute delirium tremens. When B_1 was given intravenously symptoms of delirium tremens disappeared in the presence of continued drinking.

Sydenham's Chorea. Marked improvement was noted aftar administration of the vitamin B complex in doses of 4 —8 cc orally three times a day.

Other nervous disorders. Metilde has reported complete or partial relief in six cases suffering from tabetic pains which were unaffecfed by antisyphilitic treatment. Four cases of polyneuritis of unknown origin were also treated successfully by vitamin B_1.

Jolliffe reports 150 cases of an "encephalopathic syndrome" hitherto almost always fatal ; this syndrome may occur alone or in association with pellagra, polyneuritis or scurvy. The clinical picture is characterised by clouding of consciousness, cogwheel rigidity of the extremities, and uncontrollable grasping and sucking reflexes. When 22 patients with this disease were treated with 1000 mgm of nictonic acid orally every day, supple-

mented by sodium nicotinate by injection the mortality dropped to 13.6% from 51.5% —a very remarkable result. This syndrome represented an acute, complete lack of nicotinic acid, in contrast to pellagra which is regarded as a chronic deficiency.

The vitamin B_1 requirements of children and adults may be estimated at 300 International Units per day.

Contents of vitamin B_1 (International Units per 100 gms) of some common articles:—It is present in mostly cereals and nuts.

Cambu or Bajra 110 Units, Barley 150 ,, "Cootu" 300 ,, Oatmeal 325 ,, whole wheat 180, grams 100 150 peas and lentils 150 ,Soyabeen 300, rice, raw home pounded 60, rice parboiled, home pounded 0,9 rice raw, milled 20, rice, parboiled milled 60, ground nuts raw 300, Almond 80, Walnut 150, Dried Brewer's yeast 1060—2014 Barley germ 1500, wheat germ500 1000, Rice bran 500 Oatmeal 300.

In raw milled rice practically all the vitamins which reside in the germ and pericarp are lost In parboiled rice they are retained to a great extent as they pass inside the

grain during soaking.

In hand pounding, most of the pericarp is left intact and vitamins are retained to a great extent. In chronic cases where symptoms are not urgent and vitamin B_1 injection therapy is not indicated the best and cheapest way to get supply of vitamin B_1 is through soaking polishings of rice (got in milling or hand grounding the rice) or polishings of wheat which is generally thrown away after seiving the wheat flour and known as boor, in water. In fact some manufacturers are preparing oral vitamin B_1 preparations from polishings of milled rice.

Nicotinic Acid.

Nicotinic Acid in the form of amide has a curative action in angular stomatitis with glossitis associated with various skin lesions. A syndrome characterised with pigmented dermatitis with crackling and desquamation on the limbs, mental irritability and diarrhoea together with oedema of the face and extremities yield to it.

Another syndrome with retrobulbar neuritis with glossitis, angular stomatitis, a dry scaly condition of the genitalia and pressure areas, with mild mental changes and burning feet due to protein deficiency

and pellagra are treated successfully with nicotinic acid amide (30—40 mgm) 3 – 4 times a day for 21 day.

2. *Sclerosis of the Nervous System.* The treatment of advanced multiple sclerosis with nicotinic acid and a combination of nicotinic acid and vitamin B_1 has yielded promising results in cases in which the patients have failed to respond to therapies hitherto used. More reports satisfactory response to nicotinic acid and vitamin B. Nicotinic Acid produces vasodilatation not only of the skin but also of the brain and spinal cord. Nicotinic acid and B_1 may be given par enterally in considerable doses (Nicotinic acid 150 mg), (B_1 33.2 mg) for prolonged periods without apparent harmful effects. Subjective and objective evidence of continued improvement has followed the par-enteral use of nicotinic acid and vitamin B_1.

The proper dose of Nicotinic Acid has not yet been properly determined; apparently the drug is relatively nontoxic.

Lavarello conclude that nicotinic acid is one of the most persistent, constant and intense vasodilators of the small arterioles and capillaries, and it is useful in the treatment of disorders requiring this action.

such as Raynand's disease, scleroderma, acrocyanosis and diffuse acute glomerulonephritis. It has favourable effect on cryptogenic diarrhea and constipation.

Carlos Bonorino Udaondo and Lucio V. Sanguinetli treated 19 cases of entero colitic, many of which were of long standing. Nicotinic acid exerts a sure and rapid action on the diarrheic syndromes due to inflammatory conditions of the small intestine and colon and on some forms of fermentative colitis which are not connected with pellagra.

3 Riboflavin.

Deficiency of riboflavin causes chielosis and seborrheic accumulations at the nasolabial fold. An early sign is a specific type of glossitis. The tongue is clean ; the papillae are flat rather than atrophic, and the color is definitely purplish red or magenta, as compared with the scarlet red tongue so often seen in patients with deficiency of nicotinic acid.

There are present certain ocular changes as well which can be seen easily with a slit lamp. The earliest lesion is proliferation and engorgement of the limbic plexus, which progresses to superficial vascularization of the cornea and the production of

interstitial keratitis. Photophobia, congestion of the sclera, vascularization and abnormal pigmentation of the iris, dimness of vision and actual impairment of visual acuity are relieved promptly, and at times dramatically, by the administration of riboflavin. Deficiency of riboflavin is one of the most prevalent forms of uncompensated avitaminosis. Ribolflavin is of value in the treatment of pemphigus.

Pyridoxine (Vitamin B6)

Pyridoxine is the chemical name for vitamin B (2 - methyl - 3 - hydroxy - 4, 5 - dihydroxy methyl - pyridine). Like other member of the vitamin B Complex, pyridoxine (administered both as the base and the hydrochloride) is relatively free from toxic action

Deficiency of pyridoxine. A syndrome characterized by extreme nervousness, insomnia, irritability, abdominal pain, weakness and difficulty in walking dramatically disappeared after intravenous administration of pyridoxine. It increase reticulocytes and leucocytes when administered intravenously in doses of 50 100 mg of crystalline pyridcxine in sterile normal saline. These effects were especially noted in case of macrocytic anaemia associated with pellagra or pernicious anemia.

Joliffe treated 15 case of Parkinson's syndrome. 50—100 mg) of pyridoxine hydrochloride was administered intravenously either every day or every other day. Out of this group 6 improved. Rigidity was lessened and there was increase in streugth but tremor was not affected.

Pantothenic Acid.

The "filtrate factor" is identical with pantothenic acid. Liver and kidneys of various animals are the richest source of pantothenic acid Then come rice bran baker's yeast, egg yolk, dried skimmed milk and alfa alfa. It is also essential to human nutrition and its function is associated closely with that of riboflavin.

Vitamin C.

Cevitamic acid. It occurs in all growing vegetable tissues. Green vegetables and fruit contain large quantities of this vitamin. Vitamin C is more readily destroyed by heat or oxidation than any of the other vitamins. Ordinary cooking destroys most of the vitamin C. Vitamin C disappears on keeping, even when foodstuffs are kept in a refrigerator, and, in general, it is absent from all preserved foodstuffs.

The only foods in which this vitamin can be preserved are the juice of citrius fruits and preserved tomatoes The vitamin C present in orange or lemon juice is peculiarly stable, and loses little of its potency after being heated to 100°c for an hour. The vitamin is also preserved in dried orange juice.

The major deficiency from this vitamin results in scurvy with characteristic symptoms of sore and bleeding gums, diarrhoea, oedema and haemorrhages, which may occur in any part of the body. There is also great muscular weakness. Minor deficiency is common. There is a hemorrhagic tendency from the gums and mucous surfaces along with fatigability, weakness and dyspnea on exertion. There may be anorexia and anemia and under nutrition.

Gingivitis is considered by some to be a sub-scorbutic state and acute gingivo-stomatitis and chronic gingivitis are considered by some as not due to inefficient dental hygiene or lack of the same but to vitamin C deficiency. Vitamin C in doses of 50—75 mgm. per day abolished subclinical scurvy.

Therapeutic Uses.

(1) It is useful for scurvy or subclinical manifestations of scurvy.

(2) Anorexia, anemia, and undernutrition and

infectious states if due to vitamin C deficiency.

(3) Its use is indicated in the prevention of scorbutic states.

(4) Vitam C deficiency has been found in the majority of cases of peptic ulcer. Though vitamin C deficiency does not cause ulceration but it has a deleterious effect on the healing of the ulcer. Correction of vitamin C deficiency in such cases helps the healing of ulcer. It especially helps cases with haematemesis.

(5) Large doses of vitamin C benefit cases of Psoriasis and Lupus erythematosis. It also helps healing of wounds and fractures.

(6) A marked deficiency of the vitamin existed in such conditions as pneumonia, tuberculoses, rheumatic fever, whooping cough and osteomyelitis. Vitamin C in the form of fruit juices is useful

(7) In Gold therapy reactions as haemoptysis, petechiae and urobilinogenuria vitamin C in dose of 100—200 mg. injected intravenously removed the symptoms.

(8) Treatment with vitamin C seemed to be

effective in bringing obout prope rhealing of surgical wounds

Requirements of vitamin C. A well balanced diet for school children and adults should contain some 30—50 mgm. of vitamin C per day.

Synthetic preparation is suitable for par-enteral use.

Sources of Vitamin C.

Below are given the contents of Vitamin C in mgm per 100 grammes of the foodstuffs.

Amarnath	173	Cabbage	124
Carriander	135	Drumstick	220
Cauliflower	66	Green Chillies	111
Guava	229	Lemon (juice)	39
Lime (juice)	63	Orange	68
Paprika	200	Pappya ripe	46
Pine-apple	63	Strawberry	52
Ripe Tomatoe	32	Potatoe	17

Black currents 200 mgm.

Pulses like peas, grams, etc and grains may be soaked in water and allowed to sprout for two or three days. These germinating grains can be eaten raw or lightly cooked. They may contain 10—15 mgms per 100 grammes.

Vitamin D.

The term " vitamin D " is applied to one or more substances which function in the proper utilization of calcium and phosphorus. It has been produced in crystalline form as one of the products of ultraviolt irradiation of ergosterol. It is fat soluble •

Effects produced by vitamin D Deficiency. Deficiency in this vitamin results in defective formation of the teeth and bones. This effect depends on the calcium phosphate ratio in the food The primary effect of vitamin D deficiency is to render the gut contents more alkaline than normal, and thus to interfere with the absroption of calcium Even when the calcium phosphate ratio in the food is correct, lack of vitamin D results in defective bone formation and, on the other hand, a free supply of vitamin D can correct a calcuim phosphate ratio. The derang ement of calcium absorption that results from lack of vitamin D causes a reduction in the calcium content of the blood, and this presumably is the cause of the defective bone formation. In the growing animal the bones laid down are so deficient in clcium phosphate that they are unable to support weight and bend. The dentition is imperfect. Major deficiency manifests in the form of rickets and osteomalacia.

The normal formation of the hard structures of the teeth is dependent upon an adequate supply of vitamin D, and deficiency causes dental caries. Administration of cod liver oil to children resulted in a definite decrease in the incidence of caries.

Minor deficiency. Minor deficiency is common and often over looked Mild Rickets may be present and may not be suspected. There is delay in closure of the anterior fontanelle. cranial bossing with typical bossing with square large head may be the only bony manifestation. Dentition is delayed. There are marked evidences of muscular hypotonicity and weakness. Symptoms of dyspepsia, flatulence and diarrhoea, nervous irritability and fretfulness, unnatural softness and pallor are present.

In the experimental animal. prominence of the eyes, wide palpeberal fissures, deep anterior chamber and kerato-conus were produced ; fed on deficient vitamin D, low calcuim diet. Knapp administered vitamin D and calcium to cases of progressive myopia and noted benefit in about 67% of cases who regularly took their medication, which either manifested in a reduction in their myopia or in its becoming stationary. The majority of the patients noticed increased visual acuity for distance and near

Objectively some showed better vision.

Therapeutic uses.

(1) Vitamin D is a specific in the treatment of infantile rick ts. spasmophilia, and osteomalacia diseases which are manifestations of abnormal calcium and phosphorus metabolism. Vitamin D is valuable in the prevention as well as in the curative treatment.

Treatment of rickets and infantile tetany with vitamin D. For preventive measures, is emphasized the importance of commencing early and reaching the full dose "certainly by the end of the second month" of life.

For tetany vitamin D alone is not enough. It must be given with calcium.

For premature infants and to children who had rickets parenteral administration of 500,00 to 1000,000 U. S. P. units of vitamin D was followed by uniformly rapid healing and complete absence of clinical evidence of toxicity. This is now a standard procedure.

The absorption of parenteral vitamin D depots can be accelerated by using a mixture of oil and ether instead of oil alone as solvent. Rickets and tetany respond to this form of par enteral vitamin D shock therapy as promptly as to the oral administra-

ti on of equal doses of the vitamin. Serum calcium and phosphorus become normal, usually after from 3—7 days. There is roentgen evidence of calcification in one week, and recalcification is usually complete in 30 days after the beginning of treatment Tetanic convulsions cease within 24 hours after the parenteral administration of one massive dose of vitamin D.

(2) Vitamin D helps in the healing of bone lesions in the presence of calcium and phosphorus.

(3) Vitamin D administration during pregnancy reduces the duration of labour and the loss of blood and is useful in toxaemias of pregnancy.

Toxic effects. Vitamin D is the only vitamin definitely known to be toxic when administered in abnormally large amounts. Since the range between the therapeutic and toxic dose is so very large, however, its toxicity is not an important clinical factor. Mild symptom of intoxication in children is a loss of appetite. In dose 150,000—300,000 Units may cause metastatic calcification, nausea, intense headache, profuse sweating, diarrhoea end death.

Sources. Vitamin D is formed in the skin by the action of sunlight and so the cheapest and easiest way of supplying vitamin D is by exposure of the

body to sunlight. Other sources are exposure to ultra-violet light,. Quartz mercury vapor lamps and carbon arc lamps.

Tuna liver oil	2000,000—6000,000	Units per 100 grams
Halibut Liver oil	100,000— 300,000	,,
Cod Liver Oil	10,000— 30,000	,,
Egg Yolk	200— 400	,,
Butter	10— 100	,,

Vitamin E.

Lack of Vitamin E in the exprimental rats did not affect their health and growth but yet they were unable to repoduce In the male animals there was destruction of the germcells, whilst in the female animals the ovary remained normal and conception occurred, but the foetus always died and was reabsorbed. This vitamin is fat soluble It is found in geatest abundance in wheat germ ; less abundantly in green leaves and seeds. The Vitamin is remarkably stable to heat, light, air, and to chemical agents generally but is rapidly destroyed by rancid fat. It is commonly known as the antisterility vitamin".

Bicknell found that vitamin E deficiency in rats produced ataxia which was soon followed by a flaccid paralysis with gross wasting of the muscles

of the hind quarters and back legs. The general condition, and the mentality and the appetile remained good He concluded that in the adult it is the nervous system and in the young the muscular which is most sensitive to a deficiency.

Therapeutic uses.

(1) It is useful in the treatment of sterility and habitual abortion in the female when organic diseases like gonorrhoea, syphilis, etc can be excluded.

(2) Bicknell advises its use in myopathies and neuropathies. He treated 26 case with fresh dried whole wheat germ ½ oz twice daily.

In the group of myopathies chiefly children ;the result were remarkable. Every patient improved who was treated for more then six weeks. Even bed ridden patients showed improvement.

Amyotrophic Lateral sclerosis. Not enough patients were treated for the result to be definite but on the whole they were promising. One infant with amyotonia congenita was greatly improved.

Sources of vitamin E. Richest sources are wheat germ oil, rice germ oil, cotton seed oil. It is present in abundance in green leaves and wheat germ.

Vitamin K.

Dam in 1935 showed that deficiency of a fat-soluble substance in the diet of newly hatched chicks caused a fatal haemorrhagic diathesis associated with a low plasma prothrombin level. This condition could be prevented or cured by administration of a protect ive factor which Dam called vitamin K. Vitmin K is found in the green parts of plants such as alfalfa, spinach, tomatoes, carrot tops, and oats It can also be extracted from putrefied fish meal or rice bran, in which it is probably formed by bacterial action.

Lack of fat-soluble vitamin K leads to haemorrhage and this vitamin is not absorbed from the intestine in the absence of bilesalts, and in the absence of this vitamin there is deficiency of prothrombin in the blood. If the plasma prothrombin concentration is less then 50% of normal, dangerous haemorrhage may occur. Vitamin K is of no use in the treatment of purpura and hemophilia as the blood prothrombin is normal in these conditions . The level of the plasma prothrombin depends upon liver function as well as on the absorption of vitamin K. In Laennec's cirrh-sis of liver the prothrombin level is not influenced by vitamain K as there is defective liver function present. In human intestines it is formed by bacterial-

action

Sometimes scorbutic symptoms may be due to vitamin K defeciency. Such cases are not benefitted by C but are cured by vitamin K.

Vitamin K and bilesalts are potent factors in decreasing bleeding tendencies in cases of obstructive jaundice and their use both pre-and post operatively, is recommended. However oral or parenteral use of synthetic prepration is quite effective.

Persistent haemorrhage may occur spontaneously or from trivial injuries in the newborn. During the first five days of infant's life there is a hypo-thrombinaemia. It may be as low as 30% of normal and therefore persistant haemorrhage, icterm gravis neonatorum and hydrops congenitus may result

Prothrombin deficiency is also related to the incidence and extent of intracranial haemorrhage.

The use of vitamin K in such cases raises the prothrombin level and prevents the serions consequences. Vitamin K may be administerad to the baby after birth ar to the mother during last few days of pregnancv.

When rapid effect is desired, Vitamin K may be administered to the mother less than 24 hours before delivery by par-enteral route. It is indiceted for the

mother 12 and 4 hours before delivery or for the newborn in the following cases:—

(1) In cases of maternal toxaemia.
(2) In Premature labour.
(3) Difficult or instrumental delivery.
(4) When breast feeding is not possible.
(5) When any cerebral symptoms develop during the first few days of life
(6) In cases of haemorrhagic diathesis, icterus gravis neonatorum, and anaemia.
(7) When an operation is necessary on the new born.

Synthetic preparations. The Natural Vitamin K is oil solube and is not suitable for injection. Defects of oral administration are that there may be lack of absorption due to intestinal obstruction, paralytic ileus or some other intestinal complications or it may not be taken due to vomiting. In all such cases parenternal method is useful. It is suitable for haemorrhagic diseases of the newborn. The advantage is that there is no need to give bile salts with it. With Oral administration bile salts must be present in order to assure absorption of the vitamin

This synthetic prepration is 2 methyl 1-4 Naptha quionone and is given intramuscularly in doses of

2-4 mg. This is also oil soluble.

Another preparation called vitamin K 5 has been prepared. It is water soluble and is suitable for intravenous use. It is 4—amino —2—methyl—1—naphthol hydrochloride. When it is given intravenously the response is quicker and the effect is greater. Response takes place in 3/4 to 1½ hr. and is greatest in 2 hours. There is no need to give bile salts. In patients with damaged liver it take 12 hours for the normal response to occur. Dose is 2—4 mg. There are no toxic effects even by a dose of 6 mg.

Sources. Natural one in alfa alfa grass and certain liver fats and green vegetable.

In adults probably it is synthesized by bacterial action in the colon. It is absent from the intestines of New born so long as the contents are sterile—first few days. When bacterial invasion of the bowel takes place it is formed and absorbod. Synthetic preparations are derivatives of naptho quinone.

Vitamin P

Vitamin P or Hesperidin has got action on capillary walls. Its deficiency causes abnormal capillary fragility and so petechial haemorrheges are caused. It is given by oral route in 1 gm dose daily.

Attempts have been made to give a clear cut picture of deficiency of each vitamin separately but in clinical practice deficiency is generally multiple. This is especially true in the case of deficiency of different members of vitamin B complex The several members of this complex occur together and have allied functions. The causes leading to deficiency of one member affect the others as well. For instance Pellagra is due to deficiency of nicotinic acid, Riboflavin and vitamin B_1 The psychic, some of the dermal and gastrointestinal symptoms are due to deficiency of nicotinic acid and are rapidly relieved by addition of nicotinic acid. Ocular symptoms, some of the dermal symptoms and sometimes glossitis are due to riboflavin deficiency and are not affected by nicotinic acid but rapidly improve with riboflavin. Weakness, neuritic pains, general ill health are due to deficiency of vitamin B_1. Some symptoms are common to three different groups of vitamin B complex. Possibly symptom of deficiency of other members of the complex or other vitamins may also be present.

CHAPTER II.

Hormones.

Male sex hormones. Preparations for clinical use are:— (Androgens)

1. Testosterone
2. Androsterone } and their esters,

Testosterone is six or seven times as active as androsterone. These are sterols and hence insoluble in water but soluble in oil and so are always administered in oily solution by injection. The duration of effect of the free hormone is relatively transient but of the esters, propionate or acetate, action is prolonged and so it is given twice or once in a week. Of the two esters, the activity of the propionate is both more intense and more prolonged. Testosterone propionate is the compound of choice for intramuscular injection. Oral administration of testicular extracts is practicaly without effect except that of methyltestosterone, where as, the injection of pure hormone, testosterone, by injection is twenty times as effective as oral administration. Percutaneous administration in the form of an ointment of the horm-

one or its ester requires a dose twice or three times as high as the intramuscular dose, and when given by inunction of an alcoholic tincture the dose must be six times as great. The duration of effectiveness of the hormone may be relatively prolonged (to periods of months) by subcutaneous implantation of a tablet containing compressed crystals of the hormone.

Dosage depends on the degree of deficiency of natural secretion of the hormone and on the extent of morphological and functional atrophy of the structure which have been deprived of thier natural endocrine, control. In contrast with the dramatic results which may be obtained in castrate animals and men by administration of appropriate doses of androgens are the results obtained in intact animals or human males suffering from only minor eficiencies of male hormone secretion.

The Therapeutic uses of Male Hormones.

(I) In males.

(i) Castrates.

(ii) Relative deficiency of male hormone secretion. Delayed sexual development. Cases of delayed puberty sometimes asso-

ciated with Cryptorchidism may benefit from male hormone therapy . in so for as such seconday sexual characterisitics as size of the external genitalia, growth of hair and development of a manly configuration are concerned. Gonadotropic therapy may lead to similar results and in these cases is a more logical form of treatment.

Crytorchidism is also successfully treated by Gonadotropic hormones but male hormone therapy is preferable.

(iii) In adult life. Eunuchoidism. Successful treatment of adult Eunuchoid require prolonged courses of high dosage.

(iv) Premature senility. Early failure of sexual function may constitute an indication for male hormone therapy. In the treatment of impotency which is mainly psychological in origin the use is not based on scientific basis

(v) Prostatic Hypertrophy. It has been used for enlarged prostate but the evaluation of results is doubtful

(vi) "Tonic" action of male harmones. Such

claims are completely devoid of any scientific support.

(vii) Mental disorders. Few cases have been reported to be successfully treated by the injections of testosterone propionate in dose of 5 mg —10 mg. daily or every second or third day. The treatment lasts for 4—6 weeks and improvement results after a similar period of rest. Several courses may be required. The treatment is harmless and worth trying.

(viii) Male climacteric. The effects of testosterone are most striking in the male climacteric. The nervousness. sweating, hot flushes, psychological states as despondency, melancholia and maniac depressive tendencies have been relieved markedly Thomas Hill is of opinion that the symptoms of involutional melancholia occurring in men of middle age are due to the "male climacteric" and are dependent upon deficient formation of androgenic substances. They claim great improvement in these symptoms by the injection of 10 mgm of

testosterone propionate two or three times weekly for a few months.

The use of male hormone when the testes are normal may cause a marked reduction in the number of spermatozoa in the semen.

(2) Use of male hormones in the females

The use of androgens in the treatment of female disorders is based on the acknowledged antagonism of androgen to oestrogenic action.

(1) "Chronic Mastitis" A certain group of cases with pain or general or nodular swelling of the breast are benefitted by the administration of androgens. Androgen therapy to be effective must consist of high dosage (100 mgm) weekly or twice weekly for 2—3 months but some undesirable effects such as deepening of the voice, growth of hair on the upper lips, enlargement of the clitoris may occur. The effect is only transient.

(2) Menorrhagia. The anti-aestrogenic effect of androgens which cause temporary atrophy of the endomitrium provides the basis for their use in menorrhagia. Large doses are required and there is

danger of masculinization.

(3) Suppression of Lactation by Testosterone Propionate.

In 18 out of 25 case in which the preparation was administered at the begining of lactation (approximately 48 hours after delivery) a dose of 50—75 mg. was effective in all instanses. It failed in cases in which lactation was definitely established when treatment was begin.

Female sex hormones

The Oestrogenic Hormones.

The internal secretion of the ovarian follicle is oestradiol. Its degradation product is oestrone which is found in urine of pregnancy and oestriol which is derived from the placenta. A synthetic oestrogenic hormone has been produced. It is called stilboestrol (4—4 dihydroxy-a B—diethylstilbene). It is as effective as the naturally occurring oestrogens in the treatment of pathological conditions in human patients. It is very active when given by the mouth The only untoward effects noted with it were slight nausea. It can promote full uterine growth.

Oestradial benzoate is the best form and is given

by intramuscular injection in oily solution. Oestrogenic hormones are chemically similar to carcinogenic hydrocarbons. Prolonged use of oestrogens depress gonads and gonadotropic function of the anterior pituitary and this fact must always be kept in mind during treatment with these hormones.

Preparations.

(1) Oestrone is manufactured from pregnancy urine. It is partially soluble in water and is adminis tered by mouth, by vaginal suppositories, and by injection. The trade names are oestroform, Menformon, Progynon, Tridestrin etc.

(2) Oestradial is the hormone secreted by the ovary. It is chemically identical with di-hydro oestrone which can be prepared by synthesis from oestrone. The benzoate in oily solution is used by intramuscular injection. It is marketed under different names as Dimenformon, Progynon—B oleosum. Benzo Gynoestryl, Oestroform B—oleosum.

Therapeutic uses.

(1 In vulvovaginitis. During the child bearing age, the vaginal secretion is acid in reaction due to the presence of lactic acid The vaginal discharge is pasty and healthy and the cells of the vaginal epithelieum are in highly glycogenated

condition. This era is characterised by the circulation in the blood of the ovarian follicular hormone the oestradiol which has a protective influence on the vaginal condition. In children and old women this secretion oestradiol is absent and so lactic acid is no longer found in the vaginal secretion, the vaginal epithelium becomes thin and fall an easy prey to pyogenic infections. Thus vulvovaginitis of children and senile vaginitis are produced.

(a) Senile vaginitis. Oestrone therapy is very valuable. The patient should be given in divided doses a total of about 100,000 international units of oestrone each week for three weeks. The dose should be small, frequently repeated and given intramuscularly. Stilbaestrol by mouth may suffice. At the same time a daily douche of normal saline is given. A vaginal suppository containing (1000 international units) of oestrone may be useful.

(b) Vulvovaginitis of children. An intramuscular injection of 10,000 units should be given twice a week for about four weeks. A vaginal suppository containing 1,000

international units of oestrone is introduced daily.

(2) Menopausal symptoms. These are often greatly relievec by one of the oestrogens. Severe. symptoms following bilateral oophorectomy in younger women are also relievad. An initial large dose is given by the intramuscular route at the commencement of the course followed by frequent smaller doses such as 1,000 units by the mouth two or three times a day

(3) Kraurosis vulvae, pruritis vulvae in old women also respond well to this therapy.

(4) Chronic mastitis. In Recurring painful breasts and the development of small painful areas of chronic mastitis the intramuscular injection of 10,000 international units of oestrone is given daily before and during any expected exacerbation.

(5) To prevent lactation or to arrest lactation when it has been developed after a miscarriage or even a full time delivery, the intramuscular injection of 50 00 units on each of three consecutive days is often successful

(6) Primary hypogonadotropism. Oestrogen therapy may be used in promoting growth of uterus and fallopian tube. 1.5 mg of stilboestrol dipropionate may be given daily over a period of months by mouth

or large doses of natural hormones by injection. Response should be checked by measurement with the uterine sound. A rest interval of 14 days is given after each month.

(7) Male characteristics. Sterile women with male characteristics may be treated with oestrogenic hormones which are especially indicated if the urine shows a low oestrin content. In such cases the therapy may be supplemented with gonadotropic hormone therapy.

(8) Structural occlusion of the Fallopian tubes Oestrogenic therapy by its hyperplastic effect on the genital tract may benefit cases of tubal occlusion due to developmental failure or after inflammatory blockage. Large dose are required.

(9 Failure of ovulation. Shock therapy by giving 200,000 international units of oestrin which may be injected on the tenth day of the cycle or 3 mg of stilboestrol dipropionete may be given daily on the tenth and eleventh day by mouth. After this gonadotropic hormones may be administered

(10) Acne in women is said to improve under oestrin therapy

(11) Premature babies. Oestrin therapy proves useful. 500 international units of oestrin are given

twice daily by month. Stilboestrol is not recommended It may prove too strong. The babies appear more cheerful and take their feed better and gain in weight

(12) Dysmenorrhoea. It is better to find out the cause and treat it Some cases are really due to oestrone deficiency such cases will be benefitted by oestrogenic hormone therapy.

(13) Vomiting of pregnancy. It is said to be due to deficiency of oestrone. So oestrone is given in small doses. One tablet of progynon or ovocyclin by mouth three times a day. Relief is obtained within two or three days.

(14) Pre-eclampsia and eclampsia. In these stages there is said to be deficiency of oestrone and so oestrone therapy is given with some good results.

(15) To stimulate uterine muscular effort in causing abortion or premature labour or primary uterine nertia. The use of oestrogens is not to be recommended.

(16) Cases of secondary amenorrhoea. These cases will be benifitted but the underlying cause should be treated and oestrogenic therapy should not be used indiscriminately.

(17) Amenorrhoea and sterility. Oestrin is success-

full in starting the menstrual cycle.

If the uterus is small it is advisable to given continous dosage for anything up to 6 months; this can be given orally by subcutaneous injection or by the subcutaneous implantation of a tablet of the pure hormone.

If any indication of a menstrual cycle is present, the oestrone or stilboestrol should be given for the first 14—16 days of the cycle. Stilboestrol 1—5mgn three times a day is given and then omitted for 12—14 days In cases of sterility this course is followed by one week's treatment by corpus luteum hormone.

Gonadotropic Hormones.

These Hormones are of two kinds:—

(1) One is the follicle stimulating hormone. It favours the growth of Graffian follicle of the ovary and stimulates the latter to produce oestrogenic substances. This hormone is manufactured by the Anterior Pituitary Gland but the same is not available for marketable purposes. It is obtained from the urine of women whose ovaries have been removed or destroyed or women at menapause. It is also prepared from the serum of pregnant mares or serum of

pregnant women. It is also called Prolan A.

(2) The other hormone is the lutenising hormone It causes development of the corpus luteum which is stimulated to produce its hormone progesterone. It is prepared from urine of pregnancy, the chorionic villi of placenta. It is also elaborated by the anterior gland but this is not available for the market. It is called Prolan B or A. P. L. or (Anterior Pituitary like) hormone.

Therapeutic uses.

(1) Primary and secondary Hypogonadotropisim. In the primary type these hormones seem to have little effect. In the secondary hypoplasia of the ovaries and uterus they are useful.

(2) Failure of Ovulation in otherwise normally developed women may be treated with injections of Prolan. A type hormones during the first half of the cycle.

(3) Early repeated abortion. The Luteinising action of 2nd type of gonadotropic hormones (Prolan B) may be made use of late in the menstrual cycle and following the conception and should be continued through out early part of pregnancy.

(4) Functional bleeding. This is a very frequent and troublesome disorder It is seen at the begining

or towards the close of the menstrual function, though some cases are encountered in the mid period of sexual activity. It is characterized by periods of amenorrhoea followed by long periods of bleeding. The bleeding may be constant sometimes profuse and at the other times slight. It may stop spontaneously or it may recur at intervals. In this trouble luteinising factor is deficient so Prolan B type or A. P. L or Antiutrin is given.

Dosage. By intramuscular injection. No definite dosage can be given for gonadotropic hormones. A small dose must be used to begin treatment and may be raised if no response is obtained.

Dangers and contra indications These hormones are not to be used when normal or excessive amounts of hormons are found in the urine. This may even occur in cases of hypogonadotropism.

Corpus Luteum Hormone

Corpus luteum is formed in the latter half of the menstrual cycle It flourishes till the last period if fertilisation has not taken place

ii If ovum is fertilised corpus luteum remains active until the sixth month of pregnancy.

Corpus Luteum secretes a hormone known as

progesterone.

(1) During the latter half of the menstrual cycle. It brings about a state of growth of the endometrium which is most suited to recieve and nourish the fertilised ovum

(2) During the first six months of pregnancy It continues to act on the endometrium, converting it into decidua. The action of progesterone is antagonistic to oestrone. The formation of the decidua and the decrease of the motality of the uterus are two of the most essential functions of the Corpus luteum during pregnancy

Therapeutic uses. Corpus luteal extracts do not act when administered by mouth. The most important use of progesterone is in case of threatened miscarriage and in case of habitual abortion.

Threatened Abortion A case of threatened abortion should be given the usual absolute rest in bed and sedatives. 5 International Units of progesterone are given at once and thereafter two units daily until the bleeding ceases. Subsequently two units are given once a week until the 28th week

Habitual Abortion. Progesterone is given in doses of two international units once a week as soon

as pregnancy is diagnosed, until the 28th week. At the same time a diet rich in vitamin E should be given. One capsule of vitamin E is taken daily throughout pregnancy.

Functional haemarroge In this there is excess of Oestrogenic substance and deficiency of progesterone. 5 mgm of progesterone injected daily for 5—6 injections prove very useful.

Metropathia haemorrhagica or *Anovular bleeding* There is Cystic degeneration of the Graffian follicle with no recent or functioning Corpus luteum in the ovary, also myohyperplasia of the uterus, and marked proliferation of the endometrium with cystic dilatation of the glands. Progesterone 5 mg may be injected during the bleeding phase and continued daily till it is controlled. It may be continued during the amenorrhoic phase as well.

Dysmenorrhoea. Some cases are due to increased uterine contraction and deficiency of progesterone. Such cases are benifitted by the use of progesterone.

Pre-eclamptic toxaemia. Robson and Paterson (British Medical Journal, Feb. 13, 1937) report the use of progesterone in 12 cases of pre-eclamptic toxaemia. The patients had high blood pressure systolic 160 or over and the diastolic 90 or over,

oedeme, album inuria, headache, visual disturbances and vomiting such as to suggest that eclampsia might be imminent. Progesterone was given in 5 mg doses daily for 3—4 days and thereafter, depending on tne response, at longer intervals. Out of ten, seven cases treated conservatively four developed fits and two died, while out of twelve severe cases treated with progesterone none developed fits and none died So this treatment may have some prophylactic value in toxaemias of pregnancy.

A new compound is prepared synthetically called ethinyl testo sterone, anhydro-oxy progesterone or pregneniolon. It has same action as progesterone and is many times more active by mouth. Oral dose is six times the amount of progesterone administered by injection.

Placental extract in Measles.

The extract used was Leaderles' immune globulin and it was given in one intramuscular injection of 4 c-cm into the buttocks. There were no severe constitutional disturbances or any delayed reactions. The extract did not have the effect of preventing or postponing the attack. It rendered the attack milder, the duration of temperature shorter and

lessend the subsequent complications. T. N. Parish (British Medical Journal 9, 1938)

Anterior Lobe of The Pituitary.

The Growth Hormone

This, under the name of antiutrin—growth, is available for injection in the form of 10 rat growth units per c. cm. It is extracted from the anterior lobe of the pituitary and is of use in certain cases of Dwarfism caused by deficiency of anterior lobe of the pituitary. It is administered by subcutaneous injection in doses of from 2—5 c-cm with a total weekly dosage varying from 6—10 c-cm. If there is thyroid deficiency, the simultaneous administration of dried thyroid is advisible. The treatment has to be continued over months and years.

The Lactogenic Hormone.

This hormone is also extracted from the anterior lobe of the pituitary. For initial stimulation of secretion of milk it is administered subcutaneously in doses diminishing from 5 c-cm to 1 ccm over a five day period and to stimulate a failing supply it is given for shorter periods.

Treatment of Addison's disease with desoxycorticosterone Acetate.

Addison's disease is characterised by destruction

of the adrenal cortex. This is followed by a marked excretion of sodium and chloride in the urine, a pronounced drop in the blood concentrations of these ions, an increase in the blood potassium, hemo concentration and nitrogen retention. Treatment is directed towards re establishment of a normal blood electrolytic pattern This is accomplished both with the aid of injection of cortical extract and with the addition of large quantities of salt (10—20 gm) to the diet.

Pellets of crystalline desoxycorticosterone acetate were implanted. It produced marked increase in the blood pressure but exercised no effect on carbohy drate metabolism and on the pigmentation. Dangers are hypertension oedema and heart failure.

Pellets weighing approximately 125 mg liberate from O. 20—O. 36 mg of desoxycorticosterone acetate daily.

Adrenal Cortical Hormone and Salt in Treatment of Pneumonia and other severe Infections. It is well established that the adrenal Cortex plays a significant role in the mechanism of resistance to intoxications, bacterial and protozoan infections and secondary shock. David Perla and Jessie Mamorston used cortical extract in case of bronchopneumonia

and severe influenza. Along with general treatment, from 2 to 5 cc. Cortex was given twice daily intramascularly or subcutaneously for two or three weeks until recovery. The effects noted were: (1) maintenance of normal blood pressure with prevention of collapse. (2) decrease in the evidence of toxicity, (3) avoidance of distention, (4) improvement of appetite, (5) increase in the sense of well being and (6) apparent shortening of the period of convalescence.

CHAPTER III.

Protamine Zinc Insulin in Diabetes Mellitus.

Protamine insulin and zinc protamine insulin constitute the greatest advance in the treatment of diabetes mellitus since the discovery of insulin.

In 1935 Hagedorm produced a protamine insulin suspension which on subcutaneous injection was found to be absorbed considerably more slowly than soluble insulin hydrochloride, and to possess a more prolonged hypoglycaemic action.

In 1936 Scott and Fisher by adding small quantities of zinc to protamine insulin produced a new compound, zinc protamine insulin, the hypoglycaemic action of which was found to be even more prolonged than that of protamine insulin.

Physiological Action and Composition

(a) Protamine insulin called Danish protamine

insulin, protamine insulinate; Insulin Retard.

In order to prepare this type of insulin for injection it is necessary to add 1 c.cm of a buffer solution containing sodium phosphate to 5 c.cm of an acid solution of protamine and insulin, the resulting cloudy suspension being shaken before each withdrawl. These suspensions can be prepared in two concentrations according to the strength of soluble insulin used, namely, 40 or 80 units per c.cm, and must not be kept for more than four weeks.

(b) Zinc Protamine Insulin (Protamine zinc insulin Candian protamine insulin, protamine insulin (with zinc suspension)

This is produced by the addition of traces of zinc to protamine insulin and the adjustment of the ph to 7.2. This is more stable, more prolonged in action than the protamine insulin This compound is supplied as a suspension in concentration of 40 and 80 units per c.cm, keeps well and, after shaking is ready for immediate use.

Action. The duration of action of insulins depends upon the amount injected

Type of	In doses	Duration of Action	Commonest time of Hypoglycemia	Remarks on action
Insulin	to 10 units	5—6 hours	2—4 hours	Quick and strong
	to 20 „	6—8 „	3—5 „	Balances much
Soluble	to 40 „	+ 10—12 with big dose 6—8 „		carbohydrate
	to 20 units	8—10 hours	4—6 hours	Slower, balances
Insulin Retard	to 40 „	12—16 „	6—9 „	less carbohy-
	to 60 „	occasionally 24 hours	7—12 „	drates
	to 10 units	6—8 hours	5 hours	
Zinc Protamine Insulin	to 20 „	to 12 „	8—12 „	Very slow
	to 30 „	to 18—24 „	8—20 „	balances car-
	40 units or more	24 hours or longer	16—24 „	bohydrate poorly.

In normal people the insulin requirements are: —

(1) A small continous secretion of insulin, a basal secretion, which controls endogenous sugar production and controls the fasting blood sugar.

(2) An increased secretion after meals to deal with the absorbed carbohydrate (Lawrence). In diabetics both these aspects of insulin secretion are defective but the clinical pictures vary widely with the degree of insufficiency. Mild cases, still producing some insulin, are controlled either by diet alone or by small added doses of insulin which are necessary mainly to deal with carbohydrate food, the patients own basal supply of insulin being sufficient to keep the blood sugar normal, or nearly so, except after meals. In more severe cases injected insulin is required not only to deal direct with carbohydrate food but to control the continous outpouring of sugar (and acetone bodies) in the fasting condition.

Soluble insulin is quick and strong in controlling the sugar from the carbohydrate meal following, but it is so short lived in action that one or two doses never provide a continous supply. It acts in strong waves which may even produce hypoglycaemia twice a day without preventing a relapse of sugar

and ketosis in severe cases when its action is exhausted in 6—9 hours. Zinc protamine insulin, on the contrary, provides a constant small amount of circulating insulin sufficient for a basal supply but too weak to control sugar after carbohydrate meals. It is also more irregular in its action from day to day than two doses of soluble insulin, possibly because of more irregular absorption.

All cases of diabetes suffering from coma or ketosis require soluble insulin.

The importance of various tests in Diabetic. The most important tests are:--

(1) Estimation of Blood sugar.

(2) Testing of Urine for sugar.

(3) Testing of the Urine for ketone bodies.

(1 Estimation of blood sugar. For clinical purposes it is not required It is useful in research and in diagnosis but superfluous as guide to treatment.

(2) Testing of urine for sugar. The urine can be made to yield relatively more information than blood. The finding of glycosuria indicates loss of ood in the urine, the testing of specimen passed at erent times in the day shows when this waste and points the way to the necessary modifiin treatment. It is better to use Benedicts

test as the resulting colour measures the concentration of sugar in the urine, and if a sequence of urine specimens are examined the rise and fall of the sugar level in the body is revealed.

(3) Testing of the urine for ketone bodies. A knowledge of the presence or absence of ketonuria is the most important. Ketonuria indicates that the morbid processes of diabetic metabolism hold sway within the body, and until they are under control as indicated by the cessation of ketonuria, the diabetic is in danger of being overcome by his disease in its crudest form and dying in diabetic coma. The ferric chloride test detects these substances only when they are present in quantities which indicate the imminence of coma and the nitro prusside test, which detects them in minute amounts such as occur in the early stages of balancing and in the severe relapses of the previously balanced patient. Patients in whom the ferric chloride test is positive are medical emergencies and should be treated as such; patients in whom the ferric chloride reaction is negative but the nitroprusside reaction is positive are in no immediate danger, but are as yet still the subject of grossly disordered metabolism.

Insulins

In nearly all patients who become diabetic before middle age require insulin within two years of developing the disease; of those in whom the condition appears in later life about one half come to need it.

Indications (1) It must be given to a diabetic whose urine contains sufficient acetone to give a positive ferric chloride test.

(2) It must be given to a diabetic, who, after four days treatment with a modern diet, passes urine which in the majority of specimens contains enough acetone to give a positive nitroprusside test.

(3) It must be given to a patient who, while showing no ketonuria passes sugar in all specimens after a fortnight's dietetic treatment.

Our object of treatment is to give satisfactory physical and mental health to a diabetic patient This must be measured by clinical and not by chemical standard. The patient must have a normal sense of physical health and mental well being. must have sufficient energy for his needs, he maintain his weight about the accepted normal for his height and age, and must not be to hypoglycaemic symptoms. The metabolism

of a diabetic patient may be considered under control when the urine is always free of acetone bodies and when the waste of glycosuria has been reduced to the minimum compatible with freedom from hypoglycaemic attack.

Main Principles of Treatment.

Diet. Nowadays a diet of about 2000 caloris is given containing about 200 grammes of carbohydrates. The proportion of carbohydrates, protein and fat is 2 : 1 : 1 respectively

These high carbohydrate diets are more convenient and are more palatable. They render the patient less liable to relapse. These new diets have caused the disappearance of Xanthoma diabeticorum and of diabetic dwarfism and increased carbohydrate militates against the development of the most fatal complication of diabetes.—arteriosclerosis. They increase the patients subjective sensation of health and energy. Such large allowances of carbohydrates do not necessitate proportionate increase in insulin dosage.

The protamine insulins are indicated in those cases in which nocturnal glycosuria reveals ordinary insulin has failed to control the dis

during the night; in patients in whom exercise is especially liable to produce hypoglycaemia; and when reduction of the number of daily injections is desired. The principle governing their administration is that the protamine insulins should have as their first object the control of the disease during the night, and only as their second object the restraint of the rises in the sugar content of the body which occur after meals. It is only in mild cases that the new preparations may legitimately be expected to control the disease during the whole twenty four hours. In severe case their action shall have to be reinforced by the administration of ordinary insulin at those times when a sudden influx of sugar from the intestine is found to overwhelm their mild action.

The dose of protamine insulin should be increased slowly until the urine formed during sleep is free from sugar. If when this has been achieved glycosuria persists after breakfast an auxiliary dose of ordinary insulin should be given and increased until this glycosuria is controlled.

The danger of hypoglycaemia renders it hazardeous to attempt to free from sugar the urine passed in the three hours following breakfast. We should aim at keeping a trace of sugar always in the speci-

men, and if freedom from glycosuria occurs here the dose of both the portamine insulin and the ordinary insulin should be reduced until sugar again reappears.

Zinc Protamine Insulin. Mild cases of diabetes are usually controlled by one injection of Zinc Protamine Insulin in the morning before breakfast.

The Carbohydrates in diet should be distributed evenly throughout the day and some 20—30 grams are reserved for bed time as a precaution against nocturnal hypoglycaemia. A dose of about 20 units of Z. P. Insulin is given about half an hour before breakfast, and samples of urine are tested for sugar before meals and at bed time, these specimen are almost sure to contain sugar on the first day unless the patient is abnormally sensitive to Z. P. I.

Next morning the same dose is repeated, and specimens are tested on rising, and immediately before breakfast, as well as at the other times indicated. It is important to test two specimens before breakfast as the first may contain sugar as a result of a rise in blood-sugar following the bed-time feed, and is therefore a less reliable guide to the fasting blood sugar than the second. If the second morning specimen is sugar free on two consecutive days, the dose of Z. P. I. is decreased by four units to

avoid the risk of hypoglycaemia. If the second morning specimen continues to contain more than a trace of sugar the dose should be increased by 4 units every third day until it is almost sugar free.

If this routine is carried out, most mild cases pass little or no sugar, except possibly immediately after meals, ketosis disappears, and there is marked improvement in weight and general health.

In severe cases of diabetes Z. P. I. alone fails to control the hyperglycaemia induced by ingested carbohydrates. This is achieved by using a smaller dose of Z. P. I. together with sufficient soluble insulin to control the glycosuria by day. Z P. I. plus Soluble Insulin. First a requisite dose of regular insulin is drawn into the syringe, and then the requisite dose of Z. P. I. is withdrawn without mixing the two. The ordinary insulin controls the post breakefast rise in sugar, and its action has weakned by the timeZ. P. I. is coming in to full action. For the next 6—7 hours Z. P. I. is exerting its greatest effect and thus restraining the rise of sugar following the subsequent meals. Later, the action still persisting the disease is controlled during the night.

The greatest concentration of Carbohydrate should be in the earlier part of day.

A dose of Z. P. I. is found gradually which will make the 8 a. m. Urine Sugar free (more we should not dare to give without risking hypoglycaemia at night) the glycosuria by day persists heavily in all other samples of urine. If the 8. a. m. urine is sugar free two days out of three the dose of Z. P I is large enough. If this specimen is always sugar free and if the fasting blood sugar is usually completely normal, the sooner or later the patient will suffer from hypoglycaemic attacks in the latter part of the night often just before breakfast. The dose of Z P. I is slightly curtailed

So in these severe cases the glycosuria is rectified by adding soluble inuline to the Z. P. I. as the former quickly controls the Carbohydrates taken at breakfast and lunch. The dose of soluble insulin is increased or decreased until the blood suger immediately before the midday meal is between 100 and 140mg per cent. If blood sugar estimations are not available, some idea of the correct dose of regular insulin may be obtained by testing the specimen passed immediately after lunch, the bladder having been emptied just before lunch. The mixed injection should be given immediatly before breakfast.

3. There remains a small number of patients in

whom this single mixed dose fails. Heavy glycosuria and ketosis persists towards the end of the day when regular insulin has ceased to act In such cases it is best to give a small evening injection of soluble insulin either before tea or dinner.

The very severe diabetic condition requiring the above treatment may be temporary and be due to infection or complicating factor such as worry or pregnancy, and it may be possible later to stop the evening dose and reduce the combined morning dose.

Cases requiring change from old to new Insulin.

(1) Mild Insulin Cases—for example, those having 5—15 units twice daily. This is easily and satisfactorily done by giving approximately the total previous dosage in one injection of protamine Zinc Insulin before breakfast.

(2) Cases with severe sugar and acetone before breakfast or two doses, and cases having three doses a day, and children. The alteration to Zinc protamine Insulin is sometimes quite difficult and it is done under careful control in a hospital or home. The soluble Insulin should not be omitted all at once, but

be continued in reduced amounts until the Zinc protamine Insulin exerts its full effect in some three days time. In most cases the number of injections becomes less but the total units of insulin required may be more Some very severe cases do require Insulin, they do not do well on Zinc protamine insulin.

Hypoglycaemia. An excessive dose of zinc protamine insulin produces hypoglycaemia and symptoms very similar to those from an over dose of soluble insulin. The symptoms are milder at the same level of blood sugar concentration, are slower in onset, and less obvious to the patient (therein lies a danger) but may be equally severe and even more prolonged. Such mild symptoms as headaches—especially before breakfast and those relieved by breakfast—slight nausea, general tiredness or intense drowsiness are apt to escape notice as hypoglycaemic symptoms but are quite characteristic of overdose with zinc protamine insulin and may be the only warning of a severe attack. The time of onset after injectio may be at almost any hour of the day or night, b it depends fairly closely on the dose. A dose 4 - 10 units jn a very mild or insulin sensitive

may produce hypoglycaemia three to five hours after injection but hypoglycaemia within 6 hours of injection is rare. Doses of 10—20 units are most likely to cause hypoglycaemia before tea or the evening meal, 20 to 30 units at a similiar time and also in the early hours of the night, and bigger doses later at night or just before breakfast. If a certain basal dose correctly worked out causes hypoglycaemia during the day this should be corrected by giving more carbohydrate before hypoglycaemia usually occurs. Some patients for months and years are quite happy on two doses of insulin others are careless or lead very irregular lives such should not be changed over to protamine zinc insulin. The latter class of people are more liable to hypoglycaemia with a continous action of depot of protamine zinc insulin than when two smaller doses of soluble insulin are taken before breakfast and evening meal.

Zinc protamine Insulin alone is not suitable for emergency treatment of ketosis and coma and frequent doses of soluble insulin should be given as before (probably four hourly) where rapid insulin action is required.

If hypoglycaemia occurs at night or in the early morning the basal dose is too high and should

be reduced when soluble insulin is given also, another period of possible hypoglycaemia arises some three to five hours after its injection quite apart from the hypoglycaemic action of the zinc protamine insulin.

The treatment of hypoglycaemia is the same as with soluble insulin—the giving of glucose or cane sugar by mouth, two lumps or two teaspoonfuls. Patients may take longer to recover from protamine hypoglycaemia and may require more carbohydrate later to prevent relapse from its continous action.

Advantages.

The slowness of action by avoiding sudden reduction in the sugar content of the blood minimizes the possibility of hypoglycaemic attacks. This has a great practical advantage in relation to exercise. Exercise potentiates insulin action and any diabetic taking ordinary insulin is liable to precipitate a hypoglycaemic attack by unusual exertion. These slower-acting preparation are less affected by exercise and hypoglycaemia from this influence is in frequent.

Disadvantages.

The first disadvantage.

(1) They give rise to is the severity and nature

of the hypoglycaemic attacks when they do occur. As a results of the prolonged action hypoglycaemic attacks when untreated last for a considerable time, and administration of sugar may need to be repeated many times to counteract the series of relapses occasioned by the persisting insulin effect. The mild attacks, produced by ordinary insulin and consisting of subjectivesensations followed by rapid spontaneous recovery, do not occur, for with protamine insulins the attack, once it begins, progresses to severity. A further unpleasant feature is the suddenness with which severe attacks burst on the patient. The fall of blood sugar produced by the new insulins appears to be so gentle that the warning symptoms of hypoglycaemia are not evoked and the blood sugar slides on unchecked to lower levels, where a severe attack is inevitable. The danger of such attacks is more with zincprotamine insulin than with insulin retard. Like ordinary insulin the suspectibelity to hypoglycaemic attacks is more marked in the young and least evident in the old.

The second disadvantage is attributable to the slowness with which the protamine insulins come into action. This renders them less effecient than ordinary insulin is restoring the rise of sugar in the body

and the consequent glycosuria, following the rapid influx of sugar after meals. The susceptibility of body to the action of ordinary insulin as well as protamine insulin varies at different times of the day. being least at breakfast, more marked in the evening, and most marked in the middle of the day.

It is for this reason that, in cases of any severity, single morning doses of the protamine insulin are so inefficient in restraining the rise of blood sugar and restricting the glycosuria after breakfast, and it is for the same reason that attempts to remedy this particular inefficiency by increasing the size of the single dose, to amounts which will abolish the post breakfast glycosuria, may result in hypoglycaemia either during the night or in the middle of the morning, when the body is becoming most susceptible to insulin. Realization of this point has led to the devising of a techinque designed to avoid hypoglycaemia while restricting post-absorptive glycosuria within reasonable limits.

Protamine Zinc Insulin – Report of cases in whose cases glycosuria was disregarded for one year

Edward Tolstoi & F. C. Weber New York (Archivs of Internal Medicine Sept. 1940)

Protamine Zinc Insulin acts more slowly than regular insulin. During the first three to six hours it shows little activity and its pharmacologic effect continues for at least twenty four hours with moderate doses and longer with larger ones. Reactions though less frequent are characterized by suddenness of onset and are severe and prolonged and patients have reported a definite subjective improvement.

It is possible to use a single dose of the preparation instead of the customary two, three or even four daily injections necessary with regular insulin. But it was found to be disappointing with moderately severe and severe diabetes mellitus with the diets of (200—250 gm) carbohydrates patients revealed either intermittent or continous heavy glycosuria. When the authors attempted to treat the glycosuria by increasing the dose of protamine zinc insulin, the urine became free from sugar but the patient suffered from insulin reactions at times of alarming severity.

To obtain urine free from sugar various dietary division and withholding the easily absorbable carbohydrates were tried but efforts were fruitless.

It was observed that some of the patients, though they received one dose of protamine zinc insulin a day and revealed marked glycosuria, enjoyed good health, were in fine spirits, maintaind their weight and were remarkably free from any symptoms of diabetes mellitus.

Was it at all likely that the patients' actual condition that is, his weight, his ability to "carry on" his well being and his psychic outlook, might be a more important guide than the height of the concentration of blood sugar and the glycosuria. How safe was it to allow patients to excrete large quantities of dextrose over long periods? Would they have ketosis on this regimen of one single dose of insulin with continous glycosuria The question of the effect of continous hyperglycemia and glycosuria on the frequency and severity of infections was also a consideration. They found that a patient could feel perfectly well and be free from symptoms while revealing so called poor control as evidenced by hyperglycemia and glycosuria.

Following criteria for satisfactory treatment of

diabetes mellitus with protamine zinc insulin were adhered to

(1) Maintenance of weight
(2) Absence of ketone bodies in the urine
(3) Freedom from the following symptoms;
    1. Thirst
    2 polyuria
    3 frequency of urination
    4 Hunger
    5 Weakness, fatigue
    6 polyuria
    7 pruritus
    8 visual disturbances

It was the utilization and not the excretion of carbohydrate which was of prime importance and that with patients treated as described the glyco suria was not an undesirable feature, as it protected the patient from reactions. With the use of prota-mine zinc insulin glycosuria is compatible with good therapy. Some permit 10% of the carbohydrate intake, others as much as 20%.

The authors did not even attempt to "desugarize" their patients. If the patient maintained his weight on the prescribed diet and with the single dose of protamine zinc insulin revealed no glycosuria, the

therapy was continued. However, if the patient continued to excrete sugar and revealed no evidences of loss of weight or ketosis, no effort was made to obtain a specimen free from sugar by altering the diet or the dose of insulin or both

27 patients revealed almost continous glycosuria during a year or longer. The glycosuria was deter mined qualitatively only The group was composed of the average type of clinic patient, whose health was absolutely essential for livlihood. The diet was never weighed It was always calculated on the basis of household measures and at least was only an approximation. All of the patients were instructed to take a glass of milk and three crackers or a slice of bread at bed time. They were requested to test their urine for purposes of record and were advised not to be upset if the analysis revealed sugar. They were cautioned however, that if thirst, frequency of urination or unusual hunger appeared they should report at the clinic. If the criterea for satisfactory treatment were fulfilled, i.e. if there was no loss of weight, no symptoms and no ketonuria, no therapeutic changes were made even though 4 plus glycosuria was present. If however there were a loss of weight and glycosuria, the amount of prota

mine zinc insulin was increased at frequent intervals until there was a gain of weight. As soon as they could demonstrate a gain or even maintenance of weight the glycosuria was disregarded.

A slight trace of acetone was disregarded. It was treated by the administration of salt tablets, one gm every two hours, with a glass of water for each dose. In addition hot salty broths were recommended. Usually the acetone disappeared, but when it persisted or increased one or two small doses of regular insulin usually sufficed to render the urine free from acetone.

Out of 84 patients treated in this way only 27 showed glycosuria almost constantly present during the period of treatment i.e. 1 year or more. The remaining group showed only occasional glycosuria and reveled no clinical symptoms. There were no unusual infections.

Comment.

From the study of this group of 84 diabetic patients in the outpatient department who for one year have received one daily injection of insulin and in whose cases no particular effort was made to maintain the urine free from sugar, it is seen that only 27 revealed persistant glycosuria throughout

the period of observation.

These 27 patients were in good health, and further more they were in a state of social and economic usefulness. Some gained weight even though heavy glycosuria was almost continously present. There were no complaints or symptoms at any time associated with the glycosuria, and infections were no more frequent in this group than in the group whose urine was mostly free from sugar. Diets were only approximate and only one injection was given daily in the morning. Their habits of living approximated the normal ones.

In 1914 Allen and Dubois showed that the diabetic person can and does utilize carbohydrate in the presence of hyperglycemia and glycosuria. Other workers observed that for short periods at least, the diabetic patient, irrespective of the severity of the disorder is capable of utilizing carbohydrates. Unfortunately the process did not continue. To-day one can prolong their utilization of carbohydrates by mean of insulin, so that in place of the short duration of the so called physiologic Ideal. utilization, a longer duration is produced. If this postulate is accepted hyperglycemia and. glycosuria must be of secondary importance. The most important and physiologic basis

satisfactory for treatment, therefor is not how much sugar is excreted but how much is metabolised.

Budge and Winter demonstrated that in an insulin treated diabetic person carbohydrate is utilized in the presence of hyperglycemia and glycosuria. They concluded that in view of these important findings niether the value for blood sugar nor the degree of glycosuria is an adequate criterion for the regulation of diabetes. This conclusion is particularly applicable to patients treated with protamine zinc insulin.

So the guiding principles in the presence of glycosuria and hyperglycemia are (1) maintenance of weight (2) freedom from symptoms of diabetes and (3) absence of ketone bodies in the urine.

Insulin Suppositories.

B. Brahn used suppositories of Insulin and found them of clinical value. The action of insulin introduced in suppositories sets in soon and attains its maximum after 30—40 minutes, after which it subsides rapidly.

Insulin in Treatment of Wounds.

H. Serelman used insulin in treatment of chronic wounds and obtained healing within a few weeks or

even days in patients who had received hospital treatment for several months. The procedure requires determination of insulin tolerance, excess feeding with carbohydrates and strict regulation of water metabolism. After three injections of insulin had been given one third of the patient showed marked general and local improvement. In these cases dose of 20 units was never exceded.

Insulin Treatment of Burns.

Stephen. E. Flynn used insulin externally and internally in the treatment of burns. The results have been striking in patient in shock and in whom life and death hang in balance. After setting up a reaction, 50 c c of 50% dextrose is given intravenously with 15 units of insulin.

The Insulin steps up the metabolism by helping the shocked system in catabolism of the dextrose.

Insulin applied locally on burned areas stimulates healthy granulation tissue.

Treatment of Anorexia of Tuberculous Patients with protamine Zinc Insulin

Romulo Repetto and Juan Antonio Ferrari state that administration of insulin improves the appetite of tuberculous patients and causes a marked increase in weight Every moring 10 - 30 units of protamine zinc insulin are administered.

CHAPTER IV

The Anaemias and Liver Extract. The anti-anaemic factor.

Pyloric glands of the stomach and Brunner glands of the first part of the duodenum form a secretion called haemopoietin. This factor is easily destroyed by heat and digestive juices. It is called the "intrinsic factor."

In food substances another less definitly known factor is present called the "extrinsic factor."

Both react together to form another substance called the antianaemic principle which is absorbed from the intestine and stored in many tissues eg, liver, stomach, kidneys and brain. From these depots it is supplied to the bone marrow and here its function is to stimulate the megaloblasts of the marrow to change in to normoblasts

Thus the physiological steps requisite for the normal production of normoblast in the bone marrow are :—

(1) Secretion of the intrinsic factor.

(2) Presence of the extrinsic factor in food.

(3) By the interaction of the intrinsic and extrinsic factor formation of antianaemic factor.

(4) Absorption of the antianaemic factor and its

(5) Storage in the liver and other organs to be supplied.

(6) To the bone marrow.

These steps may fail as any stage to cause megalocytic anaemia.

(1) Failure of the secretion of intrinsic factor. The stomach and duodenum may fail to secrete haemopoietin. This occurs in pernicious anaemia and other megalocytic anaemias and in some cases of gastrectomy, cancer of stomach. In Addisonian pernicious anaemia the loss of intrinsic factor is permanent. In pernicious anaemias of pregnancy the loss of intrinsic factor is only temporary.

(2) Absence of the extrinsic food factor. It may be lacking in certain tropical megalocytic anaemias and in cases of peptic ulcer undergoing partial starvation.

(3) The antianaemic factor is formed normally but is not absorbed from the intestine. Such a state of affairs is present in megalocytic

anaemias present in sprue, idiopathic steatorrhoea and Gee's disease and pellagra

(4) The antianaemic factor is absorbed alright from the intestine but liver is unabla to store it. Therefore megalocytic anaemia is seen in some case of cirrhosis of the liver.

(5) The antianemic factor stored in the liver is not utilised by the bone marrow from some unknown cause. This type of megalocytic anaemia is called by Williamson as achrestic

The resuls is that megaloblasts are not changed in to normoblasts. Immature cells escape in to the peripheral blood stream. These cells are large and well filled with haemoglobin so that the resulting anaemia is characterised by megalocytes which are hyperchromic. The bone morrow is hyperplastic.

Macrocytic Anaemias

Macrocytic anaemais are divided into two groups :

(1) Megalocytic anaemias. These anaemias develop on account of failure of the specific antianaemiac factor in any stage as described previously. The bone marrow is megaloblastic.

(2) In this group of anaemias the macrocytosis

results from causes other than a deficiency of the specific antianaemic factor. The macrocytosis is secondary in the majority of cases to prolonged stimulation or irritation of the bone marrow. Blood formation proceeds on a normoblastic basis but many larger and more immature cells than normal erthyrocytes enter the blood stream. This type of macrocytic anaemia is present in :—

(a) Some cases of haemolytic anaemia for example acholuric jaundice.

(b) Occasionally in malignant malaria and lead poisoning.

(c) In leukaemias.

(d) In case of Hodgkin's disease and malignant disease

These anaemias do not react to the specific anti-anaemic factor and liver extract injections are not required in their treatment.

So it is clear that all megalocytic anaemias are macrocytic but all macrycytic anaemias are not megalocytic. These are all hyperchromic anaemias

These two classes of macrocytic anaemia are distinguished by (i) the finding of the aetiological

factor

(ii) by full examination of the blood picture.

(iii) By their response to the specific antianaemic therapy or other forms of therapy.

Treatment of megalocytic anaemias.

Addisonian pernicious anaemia is the most common and the most important of the megalocytic anaemias. It will be used as the therapeutic example on which treatment of all the megalocyte anaemias can be modelled with minor modifications

Diagnosis. Repeated blood examinations are essential, and a "shot gun" prescription of iron and liver extract is to be deprecated. There is no alternative available to regular blood examinations for the estimation of the amount and the frequency of dosage needed for the maintenance of a normal blood level.

Objects of Treatment. The aim of treatment is (1) to restore the blood picture, qualitatively, to normal as quickly as possible (2) to maintain a normal blood level; (3) and to replenish and stock adequately the depots of the body with the factors necessary for blood formation.

Treatment The Severe Relapse stage The

patient is critically ill and in a collapsed state, with a blood count of approximately one million red cells and a haemoglobin content of 20 to 30 percent. The question of blood transfusion immediately arises. If the blood pressure is very low (Diastolic pressure of 55 mm. Hg), the pulse fast (120 or more), the heart dilated, dyspnoea present at rest and oedema severe, blood transfusion should be given at once.

Blood transfusion. One puit of blood from a suitable donor should be run into the recipients vein very slowly. 5 c cm of a liver extract specially prepared for intravenous injection (P A.F.) should be added to the blood, and 5 c cm of an extract hepatic suitable for intramuscular injection should be injected into the gluteal region. The intramuscular injection of 5 c cm of liver extract should be continued daily for 3—4 days by which time the reticulocyte increase will have started and a marked subjective improvement will be noted, within ten days the blood count should have risen by nearly one million red cells and the patient should be out of all danger.

Iron. Iron and ammonium citrate, 30 grs three times a day or Ferrous sulphate or Ferrous carbonate tablet twice or three times a day after food should

be started after the first week and continued for 2 months in all cases recieving treatment by the parenteral route, since an iron shortage is apt to arise owing to the exceedingly rapid production of erythrocytes.

Drugs. If dyspepsia or diarrhoea is present Hydrochloric acid or glycerin pepsin may be given.

The most efficacious treatment for all the symptoms of pernicious anaemia and for the prevention of such serious complications as spinal cord degeneration, and gall bladdar inflammation is the adequate administration of the anti anaemic factor.

Dyspepsia, diarrhoea, sore tongue and general weakness all rapidly disappear in the majority of cases without any symptomatic treatment.

2 Stage of moderate Relapse.

The patient complains of weakness, palpitation, exhaustion, dyspepsia and dyspnoea on effort, but there is no danger to life. The blood count may be from $1\frac{1}{2}$—$2\frac{1}{2}$ million red cells and the haemoglobin 40—60%. In such a case a choice must be made between parenteral and oral treatment.

Parenteral Treatment. An intramuscular injection of 5 c. cm of liver extract should be given on three or four consecutive days deeply into the

gluteal region, alternating from side to side. There after a weekly injection of 5 ccm must be given until the blood count is normal. It not infrequently happens that the blood level tends to become stationary around 3/½ to 4 million redcells and 80 to 85% haemoglobin and the patient looks and feels perfectly well. It is essential to restore the blood level completely to normal (5 million redcells and 100 cent haemoglolin as this is an important factor in preventing degenerative changes in the spinal cord. It may be necessary to double or treble the number of weekly injections before normality is abtained. No special diet is required. The patient should take a plentiful well balanced mixed dietery.

Drugs Hydrochloric acid and iron are indicated.

Oral Treatment

Liver extract. 500 grams of liver daily is generally needed to obtain the maximal regeneration of blood. But this is much more costly than liver extract by parenteral way and so is not recommended for economic reasons. In resistant cases and in those in whomabsorption is poor oral treatment does not compare with parenteral on the grounds of efficiency, ½lb daily

of lightly cooked liver is the average dose required if liver is taken in the crude state. Since the specific anti anaemic factor is moderately heat stable there is no point in presenting raw liver. It causes nausea and disgust.

Hog's stomach preparation.

These preparations are insoluble and contain the gastric enzyme, which is thermolabile ; hence they must not be heated. Any preparation such as ventriculin, pepsac etc may be taken I table spoon ful three times aday.

General Treatment

Patients should be kept in bed until the haemoglobin has reached aproximately 60 $^{0}/_{0}$ Chronic focal sepsis should not be treated radically until there has been an adequate response to specific antinaemic therapy.

Maintenance Treatment.

The amount of material required to maintain a normal blood level can be satisfactorily settled only by trial and checked by blood examination. 5 c c intramuscular injec tions of campolan given once every

two or three weeks is an average dose but it may vary from once a week to once every six weeks. Iron is not required if it has been prescribed during the first two months of treatment. The maintenance dose of liver and hog's stomach preparation is also extremely variable in different individuals. It may be said to be 2 lbs of liver or four ounces of hog's stomach preparation weekly.

The depot storage method of treatment. where by 5 ccm or 10 ccm of a liver extract is injected intramuscularly on two consecutive days, is of value to patients proceeding on holiday or on business to places where facilities for treatment are not available. By this method a satisfactory blood level may be maintained over periods up to 2 months Injections of liver extract (Parenteral treatment) is the method of choice at all stages of the disease.

Megalocytic Anaemia other than Addison's Anaemia. The scheme of treatment outlined above is satisfactory for treatment of the anaemia present in the other conditions mentioned with the following modifications.

Pernicious Anaemia of Pregnancy

In the majority of cases treatment can be discontinued after parturition.

Tropical and non tropical sprue and Pellagra.

In the above conditions multiple deficiencies are present which must be corrected. In addition to supplying the anti anaemic factor the deficiency of vitamins and minerals must be repaired by the administration of marmite, radiostoleum, calcium, iron For the control of diarrhoea fat is restricted.

Anaemia of Pregnancy in India. It starts in the earlier months of pregnancy as a mild normocytic anaemia and within a short time it passes through the microcytic to the severe macrocytic stage. It is not seen apart from pregnancy and there is a strong tendency to spontaneous recovery after confinement with or without treatment. In the earlier stages irontherapy and liver therapy are of great value but in the last stage when the blood picture is macrocytic and hyperchromic both these forms of treatment fail. At this stage there is remarkable fall in the blood cholestrol.

H. N chatterjee reports good results in advanced cases from cholestrol therapy. 2 C. C. m of 5 % solution of cholestrol in olive oil is given intramuscularly every alternate day. Rapid improvement follows in two or three weeks.

A note on the microcytic anemias.

The causes of the microcytic anemias are many These anemias are associated with a considerable reduction of hemoglobin and are characterized by cells of normal or subnormal size and low colour index.

Treatment The cause must be found out and removed. Iron is the sheet anchor of treatment. Marmite, protenis and vitamins may be given Liver extract is not required except in very few cases Iron must be given in the best assimilableform and in adequate dosage.

Recent Advances in Blood Transfusion.

Blood is now stored for transfusion purposes by means of an anticoagulant preservative solution. Placental blood has also been found satisfactory for storage in the blood bank for later transfusion.

Serum or Plasma is also used by transfusion in post operative shock, burns and haemorrhages with good results. Dried Plasma can be stored indefinitely in the form of powder and when re-dissolved in sterile distilled water is quite suitable for transfusion. This should enormously simplify transfusion and storage for a large proportion of cases, since no grouping of the recipient is necessary.

CHAPTER V

The closed Plaster Method of Treatment of Wounds and Fractures

Advantages.

(1) This method obviates repeated daily dressings which are generally painful and carry risk of secondary infection and toxaemia.

(2) Dehydration due to evaporation at the surface of large wound is considerably reduced which is a very important factor both in the healing of the wound and in the restoration of the patient's health.

(3) It greatly reduces the period of healing and provides a very high degree of conservative treatment of wounds and fractures.

(4) It secures immobilisation of the broken limb, but allowes mobility of the patient at the same time.

Disadvantages.

(1) It is a dangerous method in the hands of in experienced practitioner. If technique is faulty gangrene may start. Surgeons must be familiar with the closed plaster technique.

(2) If drainage on to the skin is not ample trouble will arise.

(3) In fractures there is difficulty of maintaing extension.

(4) In many cases of fractures it tends to make the correct alignment of the fractures faulty because this has to be controlled by a plaster case, which becomes loose as the swelling of the limb goes down.

(5) The bad smell which comes out of the discharge oozing out.

(6) Septic dermatitis may occur.

(7) Skin which grew after the healing of the wound beneath the plaster was poor, often, ridged and thickened,

The method is suitable for injuries to soft tissues in case in which there is much loss of substance as well as to fractures.

At Barcelona about 5000 wounded persons almost all fracture cases were treated in one year. There were oniy 26 cases which required seconday amputations. There were 37 deaths among these cases 15 due to gas gangrene, 17 due to septicemia and five to secondary haemorrhage. There was no instance of non union or mal-union resulting from a faulty

position of the callus of the fracture despite the fact that in a certain number of cases of comminuted fractures there were a great many broken pieces that had lost all nutrient connection. Some cases of non-union have been in the forearm due to extensive loss of substance due to the shattering of the bones.

Indications for the closed method of Treatment.

(1) At an Early stage. The closed method is recommended for cases in which it has been possible to clean out and excise the whole wound thoroughly within six hours of time it was received. Tha more extensive the wound the greater the advisability for using the closed method. If the wound has been sutured. either partially or compeletly, it is important before enclosing the limb to make sure that there is no tension in any of the wound strata. Haemorrage must be controlled before the limb is enclosed. There should be no haematomata.

The method is contraindicatad in the following cases:—

(1) When there is any risk of extensive necrosis, due to the severity of the contusion and inadequate circulation.

(2) When the wound is unsuitable for saucerizing.

(3) When a vascular lesion or the slightest suspicion of the existence of such a lesion is present

(4) When there is severe crushing.

(2) At a later stage Infected wounds or wounds in which there is much dead tissue should be enclosed in plaster provided that they have first been submitted to debridement and saucerization.

Technique. The Cavity of the excised wound should be lightly packed with sterile guaze, some use petroleum Jelly. Sulphonamide solution saturated gauze or sulphonamide crystals (sterilised by auto clave) implanted in the wound before the application of plaster gives very good results. Similarly zipp (zincoxide, Iodoform and petroleum emulsion) may also be used

A plaster bandage applied direct to the skin then immobilizes the limb. The plaster should be moulded carefully over all bony prominences to ensure the greatet possible immobilisation and should enclose the two joints nearest to the wound. In cases of wounds in soft parts with destruction of tissues but no fracture of bone. the same technique should be used

If there are no obvious signs of trouble, every

plaster should be retained in position for a period of from 3—6 week without any window or opening being made in it.

If the plaster has to be removed it should be opend in to two halves and wound exposed to the air for 3—4 days so that the dermatitis which sometimes appears may be dealt with. After this interval when the condition of the lesion permits, a new plaster is applied. Throughout the whole period during which the plaster is in position a very carefull watch must be kept on the patients, general and local condition. The discharge may be very free and may stain the plaster and even ooze through to the outside It is of no importance unless an unmistakeable smell of putrefaction is present which indicates the presence of a form of necrosis and demands an immediate modification of treatment. If maggots, should appear in the plaster it is a matter of no great significance Local indications are a good circulation, and range of movement in the fingers and toes, the absence of odema a normal temperature in the region of the wound and freedon from all discomfort.

Blood count, the leucocyte count and temperature of the patient should be closely watched. Systematic radio graphs should be taken to make sure that the

fracture has been correctly reduced.

Complications. The chief complication that may follow fracture wounds is septicaemia. Septicaemia does not occur when the granulations are completely impervious.

Examination of the wound. In cases progressing satisfactorily the wound is found to be granulating freely when the plaster is removed. The granulations are deep red in clour and bleed very readily. Epithelium forms far more quickly than it does in wounds treated by the open method

The disadvantage of this treatment is the repulsive smell —sour and butyric —given off by the discharge. If, however, a smell of putrefying tissues is noticed the plaster must be removed

The first indication that the clinial picture is not satisfactory is a deterioration in the patients' general condition, followed by pain and a sensation of tension in the region of the wound. The plaster becomes hot and a stubborn diarrhoea often sets in

Temperature. In the first few days after the application of the closed plaster the temperature, rises even if the patient has previusly had no fever It then falls by lysis in the course of the next four or five days. A similar rise of temperature follows each

application of new plaster after a break in the treatments.

Sedimentation Rate. It is always very high at what ever period it is recorded and even when the patients' clinical condition is excellent

Total and Differential Leucocyte Count. The total leucocyte count is very high at the beginning of treatment or if sepsis is present. It falls with the fall of the temperature. Differential count which first indicates a state of suppuration soon changes. Poly morphonuclear leucocytes, after a preliminary increase to 80% decrease to a normal number and Arneth's deviation disappears. The appearance of lymphocytosis and monocytosis indicates that the wound is cooling.

Treatment of wounds with Urea (carbamide)

Urea has proved very valuable in the treatment of wounds for the following reasons :—

1. Urea in aqueous saturated solution, by its power of dissolving necrotic debris, removes the chief deterrent to healing in many types of chronic infection.

2. It is almost totally non-irritating to living tissue.
3 It is mildly bactericidal to many forms of organisms especialiy those producing putrefaction.
4 It almost immediately eradicates all odour without producing another odour.
5 It is inexpensive.

The practical difficulties in the use of urea for the purpose of wound healing are two : -

(1) Saturated solutions or crystals of urea have a tendency to dry out and cake on occasions and so there is difficulty ofmaintaining them in proper contact with the tissues at times.
(2) Hypertonic solutions of urea are painful to denuded tissues.

These difficulties have been overcome by the use of a paste containing Carbamide 50.0 percent, Indian gum 2.5 %, Eucupin 0.5% and is compounded as follows : -

500 grams of urea crystals are dissolved in approximately 300 cc of hot water. Half of this solution is then placed in another container and 25 grams of powdered Indian Gum are dissolved in it by vigorous stirring. The resulting paste is then

sterilized by autoclaving. To the other portion of urea solution 5 grams of "Eucupin" dihydrochloride are added and this mixed with the autoclaved urea-gum-solution and made up to a final volume of 1000 cc. This paste on cooling is ready for use

"Ecucpin" acts as a local anesthetic and may be omitted if pain is absent.

Saturated urea solution may best be applied in empyemata, nasal sinusitis and chronic ottitis media. fistulous tracts as in chronic osteomyelitis. post operative rectal fistulectomy, ischio rectal abcess cavities, and in deep infected wounds

Urea crystals or paste may be used for seriously contaminated, traumatic wounds involving soft tissues, tendons, blood vessels., bone and joint surfaces.

Dilute solution of urea are to be avoided as they provide an excellent medium for bacterial growth. The chief value of the compound in wound healing is due to its remarkable solvent action on necrotic tissue.

(*Holder. The annals of Surgery July 1939*)

CHAPTER VI.

Shock Treatment of Schizophrenia.

The idea of shock therapy for the treatment of schizophrenia arose from the idea that epilepsy and schizophrenia were biologically antagonistic as epilepsy and schizophrenia were said never to occur together. The opinions about the advantages or disadvantages of this therapy are divergent There are critics who condemn it as barbarous and dangerous. All sorts of serious and alarming symptoms. such as status epilepticus, Coma, convulsions, cramps, tetany, laryngeal and bronchial spasm, exhausting sweating, loss of reflexes, paralysis of the heart and, respiration, collapse, violent restlessness. hemiplegia tremor and twitchings rapid pulse, cheynestokes breathing, oedema of the lung even death have been reported during shock therapy.

On the other hand many competent observers have reported satisfactory results.

All sorts of results have been reported. Cures from 5% to 30% and improvements from 10% to 75 per cent. But any how shock therapy has a definite place in the treatment of schizophrenia.

Older methods of treatment consisted in the sudden letting of a patient down through a trapdoor in the floor, putting him in a whirling chair, suddenly douching him with cold water. Newer methods consist in the use of insulin, cardiazol and other drugs.

In all the methods mentioned or tried both old and new, whether it be a trapdoor or insulin, shock is a constant factor and a chemical substance always associated with shock is histamine. In fact, histamine is not only present in insulin shock but in every variety of shock, including anaphylaxis, surgical shock the shock of acute intestinal obstruction and the shock of extensive burns.

A lot of the poisonous symptoms seen during shock therapy can be shown to be a mixture of the symptoms produced by poisonous doses of insulin and histamine. Hill tried non toxic doses of insulin and histamine with the same results as with the convulsion method. He advocates use of non-poisonous doses and repeated small shocks with-out injuring the tissues and without a fit instead of giving a patient a poisonous dose of substance and a shock which causes "massive injury to the tissues" This treatment has also shown good results in other cases as manic-depressive, melancholia and especially in stupor. Insulin and

cardiazol form the basis of shock therapy now being largely used in the treatment of schizophrenia, and the results are distinctly encouraging. Insulin treatment is considered to be more suitable for the paranoid and and excited types, while the stuporose type reacts more readily to cardiazol.

Insulin or Hypoglycaemic shock Therapy

This treatment was first introduced in 1933 by Sakel. His technique is still used with slight modifications.

Patients selected for treatment should be free from serious physical disability. in particular cardiovascular disease. Early cases up to one year in duration and paranoid in form are the best from prognosis point of view. The physician and a staff of trained nurses are required to be constantly present in order to safeguard the ominipresent dangers

The treatment is divided in to four stages :—

(1) Finding the shock dose of insulin

(2) Giving daily injection of this dose until improvement has occurred.

(3) Rest period when no treatment is given

(4) Period of stabilization during which amounts of insulin less than the shock dose are administered, or else hypoglycemia is inter-

rupted before the full effects have been produced.

The treatment begins at seven in the morning with the intramuscular injection of 15 units of insulin in to the fasting patient. If it does not give rise to coma the dose is gradually increased by 5 or 10 units on succeeding days.

The average dose necessary to produce coma is from 60 - 80 units but as much as 300 units have been given. Hunger, sweating and somnolence gradually developing in to coma make their appearance. If muscular twichings or epileptiform attacks occur the treatment must be stopped. Coma usually comes on during the third hour following injection and is characterised by relaxation of the entire musculature end inability to react to sensory stimuli. An optimum dose has been attained when the corneal and planter reflexs are absent. Coma is usually terminated after about 1½ hours to 2 hours but this time is suited to the individual requirements.

Interruption is normally carried out by giving 150-200 grammes of glucose in tea, milk or water through a nasal tube and funnel. A sufficient amount of carbohydrate food must be taken during the remainder of the day to avoid recurrence of hypoglycaemia. The duration of treatment is from 60—90

days but it may be prolonged in cases of long standing. A 33% solution of glucose should be always at hand which must be given if any complication occurs. These complications are—epileptiform attacks, spasm of the limbs in hyperextension, feeble irregular and rapid pulse, collape, laryngeal spasms with cyanosis. The mortality has been estimated at only 1.5%

Cardiazol or Convulsion Therapy. This treatment was introduced by Von Meduna of Badapest in 1934 as the result of his observation that schizophrenia and epilepsy rarely occur together in the same patient. He used at first camphor and then metrazol. Early cases with sudden onset are the best to respond. Catatonic or stuperose has the most favourable prognosis. The patient should be free from organic diseases of cardiovascular, renal or respiratory systems. Acute febrile illness and pulmonary tuberculosis are contra indications

Cardiazol is injected intravenously in 10% solution. The initial dose is 5 cc for men, 4cc for women. If this be sufficient to produce a convulsion it is repeated on the next occassion if not, it is increased by 1 cc at each subsequent injection until the convulsant dose is reached. Convulsions are produced two or three times a week and 30

constitutes a full course.

The treatment is best given in the morning on an empty stomach, and the bladder should be empty. At least one assistant is required to attend to the mouth. The dose of cardiazol is injected intravenously as rapidly as possible—in fact success depends largely on the speed with which this is done.

In 10 –20 seconds the fit begins with sudden pallor, a characteristic short cough and twitching of eyelids, facial muscles and hands, followed immediately by generalised tonic and clonic convulsions as in an ordinary major epileptic attack. At the begining of the tonic phase the mouth opens widely and the opportunity is taken to insert the gag.

Patients undergoing this treatment, like epileptics acquire voracious appetite and gain in weight.

Complications. These are few the most important being thrombosis of the vein, dislocations especially of jaw and shoulder. To avoid venous thrombosis a substitute for cardiazole—triazol may be give intramuscularly.

Combined Therapy. Often cases which do not respond to one method respond to the other

In order to obtain the maximum therapeutic effects therefore, various combined methods have been devised. These are :—

(1) Alternating Insulin for five days and cardiazol on the sixth.

(2) Insulin course is followed by cardiazol and then repeated.

(3) Cardiazol 1½ hours after insulin or summation treatment.

Results. The spontaneous remission rate of the disease is about 30%.

Insulin therapy shows a 60% remission rate for cases of less than one year's duration. This falls to under 30% for cases who have been ill from one to two years.

Cardiazol Therapy. Von Meduna claims 50% remission in treated cases of under one year's duration.

Convulsion Treatment of Early mental illness in outpatient clinics.

Horsley (the Medical Press and circular January 1940) advises treatment of early mental illness in out patients clinics. He used Cardiazol, triazol and picrotoxin.

Out patient Technique. Method is to induce a

series of single convulsions at intervals of 3—4 days. The injections were given betwee 3—4 oclock in the after noon, the patient being allowed to have a normal breakfast, but only a very light luncheon. The treatment was given with the patient lying on a couch. Clothing was loosened and outer garments such as coat, collar and shoes were removed. Intravenous injection of cardiazol is given. Following an effective injection of cardiazol the paroxysm was almost instantaneous. After this the patient is encouraged to rest quitely for an hour and kept under observation, and then, if fit, he is allowed to be taken home. It was given in 10 cases

The Triaz l series. The initial dose for an average person was 1—2 ccm of a 5% solution given intramuscularly.

This dose may be increased or decreased according to its effect. The action of triazol is slower than that of cardiazol, and there is commonly an interval of a minute or longer before the convulsions. This dose usually produces one convulsion. If the dose was ineffective it was increased to 1·5 cc— on the next occassion and if this was also ineffective it was increased at subsequent visit by increments of 0·2 ccm. An average number of 10 injections are

required.

The author treated 8 cases with triazol with recovery in sixcases.

(3) Picrotoxin. Picrotoxin is used in an aqueous solution of a 0·3% . The initial dose is 4 ccm given intravenously. It is increased gradually if necessary by 0·5 ccm. The injection is given slowly. The onset of paroxysm is gradual. It begins with pallor and prolonged intermittent twitching, begining in the eyelids, and facial muscles and spreading to the arms, to be followed after a variable interval of about one hour, by atypical major convulsion. The whole reaction is much less unpleasant for the patients. Some 22 cases were treated by the author with recovery in 18 cases.

Picrotoxin is free from unpleasantness sometimes associated with Cardiazol and Triazol and so it is the most suitable convulsant yet used in the shock treatment of certain mental illnesses.

CHAPTER VII

Treatment of epilepsy with Dilantin

Sodium diphenyl hydantoinate or dilantin (epanutin, solantin) is a compound closely related to nirvanal. It is unfortunately more toxic than the barbiturates and toxic rashes commonly occur, as well as untoward nervous symptoms such as ataxy, tremors, and diplopia. The margin of safety between the therapeutic and toxic effects is small, but the toxic symptoms are rarely serious and with temporary withdrawal of the drug they rapidly disappear. It is more effective in grandmal seizures than those of petitmal.

Dosage. The drug should be introduced gradually without sudden withdrawl of previous medication, bromides or barbiturates what ever they may be. Two capsules each 1½ grs daily may be useless, 3 may prove to be perfect therapeutic dose, and 4 may give rise to toxic signs and symptoms. The drug is less hypnotic but more anticonvulsant. Generally increase of dose after prolonged use is not required and no diminution in the efficacy of the

treatment has been observed and no signs of mental deterioration have been observed. It is not cumulative in action.

Results. Butler treated 43 cases. 46.5% were greatly improved, 16.28% should some improvement. In all 63% derived benefit from the treatment. Improvement is much more noticed in psychological symptoms. Patients appeared brighter and more intelligent and less introspective. Some of them felt so much better as to say they have "begun a new life". Even in those cases in which no improvement in the incidence of fits has been recorded, the patients say that they are happier and more alert.

If no favourable results ensue in the course of 2-3 weeks the treatment will prove ineffective

The drug is more rapidly effective when given before meals. It is strongly alkaline in reaction and should be taken with at least half a glassful of water to minimize gastric irritation. If there is gastric intolerance the drug may be given with or immediately after meals.

Toxic Symptoms. Tenderness and sponginess of gums may appear. Fever, dizziness, impaired vision and ataxia are frequently encountered but

disappear usually with reduction of dosage and as a rule do not reappear as the dose is increased again to an effective level.

Serious manifestations are dermatitis and purpura and are indications for discontinuing the drug.

i. Nervous symptoms of intoxication may be dizzinen, giddiness blurring of vision, diplopia, clonic spasms, tremors general muscular irritability, ataxia and nystagmus

ii. Mental symptoms may be euphoria exitement agitation, irritability, confusion, delusions, hallucinations, dullnen, depressian and suicidal tendencies.

iii. Skin manifestations rashes may be erythematous scarletiniform, or morbilliform These may be very severe and accompanied with fever. There may appear exfolative dermatitis also.

iv. Gastrointestinal symptoms may be nausea, anorexia abdominal discomfort constipation etc. There may be spongness and tenderness of the gums. Thera may also be epistaxis.

Treatment of toxic symptoms. The drug should be immediately and completely withdrawn. If the toxic symptoms disappear within a few days, the treatment with the drug may be started again. The starting dose should be small and be increased gradually.

CHAPTER VIII

Calcium Acetyl Salicylate

Calcium salt of acetyl salicylic acid has the following advantages over ordinary aspirin.

(1) A neutral salt—free of acidity The ordinary aspirin is a fairly strong acid substance. The acidity of 15 grains of aspirin is equivalent, if taken three times to that of about 160 cc of a decinormal solution of hydrochloric acid. So excessive and prolonged use of aspirin is likely to give rise to acidosis. As the drug is excreted by the kidneys' they are liable to be irritated by the drug especially if already inflamed. Calcium aspirin is devoid of this defect even in large doses.

Intensive aspirin therapy conducted over protracted periods tends to disturb the normal acid base equilibrium of the body It may result in decalcification of the bones and cartilages.

This would be very serious in the case of certain types of arthritic patients and is also a point of great importance for growing children and for women during pregnancy and lactation. Calcium aspirin,

being neutral is free of those drawbacks. It is a good source of assimilable calcium and therefore it possesses several definite advantages in these special circumstances

Ordinary aspirin is badly tolerated by certain gastric sensitive patients with resulting nausea and vomiting.. It is contraindicated in cases of gastric duodenal or intestinal inflammation or ulceration In idiosyncratic persons it may produce palpitation swelling of the lips and face, oedema, urticaria extreme depression and even asthmatic attacks. In such persons calcium aspirin is generally will tolerated.

(2) Very low toxicity. Calcium aspirin exerts no adverse influence on cardiac action and is much less toxic than aspirin. In conditions calling for very intensive salicylate therapy, calcium acetyl salicylate is definitely very much safer to employ than ordinary aspirin.

(3) Ready solubility The solubility of ordinary aspirin in water is low 1 m 300. whereas that of calcium acetyl salicylate is 1 m 5. Its ready solubility and non irritant character renders it emminently suitable for the purposes of injection, per rectum or intravenously.

For Intravenous injection 1 gram in 20 ccs or a 5% solution is used and injected slowly and without delay.

For per rectum injection. Dissolve 1 gram in 1-2 ozs of lukewarm water and administer without delay.

Calcium aspirin is much more readily absorbed than aspirin and is more slowly eliminted from the system Therefore its action is much more sustained

(4) Availability of calcium and its value. The amount of calcium present in calcium acetyl salicylate is approximately 10% and this is available for maintaining a healthy calcium balance. So it is of particular importance for growing children and for women during pregnancy and lactation, when there are considerable increase in the normal calcium demands of the body.

Calcium aspirin is very useful in the treatment of chorea and dyspeptic patients.

The drug is readily hydrolysed and is an unstable product. It is inadvisable to prescribe calcium acetyl salicylate as a solution which may have to be kept for any length of time.

When calcium aspirin is mixed with 5% calcium chloride and 1% sodium chloride a fairly stable

product least liable to contain free salicylic acid results When this product is kept under normal conditions in well stoppered containers, it posseses a very high order of stability approaching very nearly that of ordinary aspirin itself.

(Green Coplans, Gellman and Medical Press and Circular.)

CHAPTER IX

Pharmacology and Therapeutics of Snake Venom.

The snake venom is generally got from two different varities of snakes and so it differs in its pharmacological and therapeutic action from each variety.

(1) Cobra Venom (2) Russel's Viper Venom.

Cobra Venom. It has a depressant action on the central nervous system, particularly on the respiratory centre and on the nerve terminals in the muscles. Its action appears to be limited to some subcortical region or synapses, with no spread to the Cortex and the Central mechanism controlling the special senses of sight, hearing and smell in contradistinction to the effects of morphia. Cobra Venom not only increases visual acuity but markedly widens the field of vision, especially for green and red. It has a destructive action on the granulation tissue. It caused a rapid disintegration of the cells of adeno-carcinoma if injected in to the tumour itself. Besides

analgesiac effect Venom of cobra has got some deep effect upon metabolic processes in the human body.

It is said to be useful in delirium, hallucinations, aphasia and melancholia and some improvement has been claimed in apoplexy, meningitis, hysteria and chorea.

On account of its depressing effects on the sensory nerve endings it has been injected inside the tumour to stop the pains of inoperable carcinoma. It is useful in the severe pain of malignant tumours, sciatica, tabes dorsalis and neuralgia. It was found to relieve pain in cases of rheumatoid arthritis, spondylits, degenerative arthrosis and there was also a considerable functional improvement in the affected parts.

Most significant of the results are those in treatment of tabetic crises and tic doulourex. In 20 cases of Macht, the pain was relieved by cobra venom in 15.

W.T. Black treated 17 cases with cobra venom.

The majority suffered from advanced carcinoma of the Cervix. The treatment of choice consists of injections of 2½ m u. for the first two days and 5 m.u. there after until the pain begins to subside. Then the injections are given with diminishing frequency, the dosage being ultimately limited to an amount sufficient to keep the patient comfortable. The venom proved to be an effectual agent for the relief of intractable pain. The patients exhibited no tendency to habit formation. The venom caused no disturbances of liver or kidney functions, impairment of circulation or alteration of blood cell morphology. Butler advises the use of a cobra venom preparation called Venomin by intradermal route never hypodermically, intramuscularly or intravenously so that it is absorbed slowly. A tuberculin syringe with a 25 gauge needle is the ideal thing to be used for injection. Butler tried it in 25 cases including cases of herpes zoaster, arthritis, neuritis, burns, injury, neuralgia etc. Marked improvement was seen in 90% and symptomatic cure was obtained in at least 85 % of the cases. Injections were made at intervals of 3-7-10 days.

A dose of 0.001 mg relieved the pain of malig-

'nant tumours in patients who otherwise needed large doses of morphia for relief. The injection of cobra venom only needed to be repeated every 8 th or 10 th day. Macht treated 105 cases of carcinoma of various parts of the body. He started with 2—3 m.u and then gave a full dose of 5 m.u. intramusculary daily till a relief of pain was obtained. At first an initial dose was given to see if there was any idiosyn crasy to snake venom and later the dose was increased In 38% of cases, a marked relief was obtained ; in 28·6% definite amelioration; 21·9% slight relief ; in 7%doubtful and in 9% no relief. The relief of pain was due to the action of the venom on the higher centres resembling that of morphine action but there is no danger of habit formation.

Dose of cobra venom is (1—10 mouse units). The smallest dose is given to begin with. It is increased slowly. Injections are given twice or thrice weekly sometimes after greater interval. Usually ten doses are required,

(2) Russel's viper venom or Indian Dabios venom. The action is mainly on capillaries and is similar to that of histamine shock. It acts on the circulatory

system. In high concentration it retards the coagulation time of blood. But in high dilution it acts as coagulant and on account of this property it is used successfully locally in stopping the severe bleeding of haemophilia, local oozing of blood in after operations and as a good coagulating plug in cases of severe bleeding wounds and after extraction of teeth "Stypven" B W & Co, in a solution of 1 in 10,000 is useful in cases of extensive bleeding from the wounds

CHAPTER X.

Modern Treatment of Burns.

General Principles governing the treatment of burns are:—

I. The first aim is to save life.

II. The second is to avoid infection.

III. The third to prevent deformity.

If life is endangered the consideration of paramount importance is the prevention of shock. This is done by maintaining the body temperature and by the administration of a sedative and by intravenous plasma or serum.

Local Treatment. For extensive burns of whatever degree the following lines of local treatment are advised.

Under a general anaesthetic gas and oxygen or pentothal the burn areas are thoroughly cleansed by the gentle but liberal use of soap and water This is followed by saline and deberis is removed completely under strict aseptic precautions (Soft soap is avoided; it is better to use soap flakes). No violent scrubbing is to be used and antiseptic

solutions or spirit are best avoided. If the burnt area is impregnated with oil or grease, ether soap is of value. For cleansing extensive burns should never be exposed at one time, owing to the risk of increasing shock by loss of body heat; a limited area only should be exposed for treatment, which should be completed before the next area is treated. Loss of heat is especially marked after the use of ether soap. After the cleansing, the burn surface and the skin around should be dried and dusted lightly with sulphanilamide powder; a coagulant is then applied, except on

1 The face
2 hands and wrists, and
3 feet.

Coagulant Applications

The following solutions are the most suitable, as they act quickly and require no special apparatus

1. Silver Nitrate 10%
2. Tannic Acid 10%
3. Silver Nitrate 10% and tannic acid 5% used alternately
4. "Triple dye." (One formula in Common use is gentian violet, 1 in 400; brilliant green, 1 in 400; with neutral acriflavine, 1 in 1000. The

solutions are mixed in equal proportions).

The application is made by the use of a large gauze mop; no dressings are required over the coagulated area, but the part may be covered with a sterile towel after the coagulum is dry. The edges of the area and any cracks developing on the surface should be dusted daily with sulphonamide powder. The coagulum must cover the whole area and a good margin of unaffected skin around, and must be firm and dry or else the effect of the treatment is nullified by the loss of fluid from the burnt area.

Treatment of Burns in Areas which should not be tanned. (Face, the hands and wrists, and the feet) Tanning in these areas carrys the risk of dangerous constriction of vessels or distortion of tissues.

A so called "tulle gras" is prepared as follows: Curtain net with a mesh of 2 mm is cut into pieces 9 cm square; these are placed in a tin box of slightly larger size, and the box is filled with a mixture of soft paraffin 96 gramms and balsam of Peru 2 gramms, sufficient to impregnate and cover the material completely after sterilization by heat in an autoclave.

The burnt area is cleansed as described above

and dried and dusted with sulphanilamide powder. A "tulle gras" dressing is then applied which is covered by 6—8 layers of gauze wrung out in warm normal saline. The gauze is kept constantly moist by warm saline being dripped on it from time to time and it is not to be allowed to become dry under any circumstances whatsoever. For the first few days the gauze may be changed every three to four hours, but the tulle gras is left undisturbed during this interval. Twice a day at first, and subsequently according to the progress of the case, the tulle gras dressing is changed

Dressings must be carried out with full aseptic technique. An oil silk or jaconet bag or cover may be used to keep the gauze moist in the case of arms and legs.

Use of a Glycerine-Sulphonamide Paste ("Euglamide") in treatment of Burns.

Robson and Wallace point out the limitations of coagulating methods in the treatment of burns (British Medical Journal March 29, 41).

Tanning of burns of third degree has always resulted in infection and made subsequent skin grafting difficult. Burns of face are not suitable for coagulent treatment because deformity may be

produced. Burns of the hands if treated with tannic acid give the most unfortunate results and so this coagulating method is not to be advocated in their treatment. Oedema and sepsis under a rigid tan, together with prolonged immobilization produce limitation of movement, contracture and in some cases ischaemic necrosis.

The authors advocate the use of the following paste to meet these difficulties.

5 grammes of soluble albucid powder is mixed with 100 c cm of glycerine; the mixture is then heated cautiously until the solid is completely dissolved. The heating is then discontinued and 10 c cm of cod liver is added, and is thoroughly stirred in This solution is mixed into a quantity of fine Kaolin (about 80 grammes) sufficient to yield a smooth paste of the consistence of thick cream. The mixing is done in a mortar, and, later, on a white slab with a spatula.

Technique of Application.

An anaesthetic may be required for cleansing but this is not essential, except in children in whom fear and apprehension are prominent. The burnt area is cleansed with warm normal saline, blisters and loose epidermis are snipped and removed and

all foreign material removed

In applying the paste a thick spread is made on sterile white lint, guaze, or linen; for burns of the face a mask is cut out Further dressing is applied if necessary and the whole is covered with wool and bandaged. In burns affecting the face and in the region of flexures the paste and dressings are re-applied daily, but in other parts they may be kept on for three days before being changed. In infected cases daily re-application of the paste be made. At each change of dressing the affected part is wiped clean with wool pledgets soaked in normal saline or cod liver oil.

Pain was experienced on application of the paste in only a few instances, and irritation was absent As a rule an early healing surface was obtained.

In extensive burns the euglamide method has not been used; possibly in such cases the application of a coagulating agent i e. tannic acid is essential to combat secondary shock.

CHAPTER XI.

Intravenous Anaesthesia.

Introduction of intravenous anaesthetics is a tremendous stride forward in medicine. The most commonly used drugs for this purpose are evipal and pentothal sodium. The solution of the intravenous anaesthetics should be as dilute as possible. Their use is two fold:—

(1) For basal anaesthesia or as a method of premedication.

(2) As a complete anaesthetic.

Pentothal Sodium. It is a lemon yellow powder, readily soluble in water, its solution being alkaline in reaction, and having a faint greenish yellow colour If solutions do not become perfectly clear, or contain an insoluble residue, after a few seconds they should be discarded. It powerfully depresses the respiratory centre, affecting the amplitude rather than the rate of respiration. Therefore an apparatus for the administration of oxygen or oxygen 95% or Co_2 5% should be available. An adequate airway must be maintained. Overdosage from too

rapid administration or from excessive amounts readily produces cardiac, hepatic and cerebral damage from anoxia. Laryngospasm, trismus, sneezing, coughing, and hiccup occasionally occur even during deep anaesthesia. Prevention and relief are readily obtainable by the injection of atropine. It does not affect the kidneys, and so renal disease is no contraindication unless it is far advanced. During surgical anaesthesia the skeletal and corneal reflexes are abolished. The pharyngeal reflex is unaltered. Vasodilation usually occurs. It has no direct action on the heart.

There is generally a fall in blood pressure, though this is rarely marked. When properly administered pentothal sodium causes little change in the pulse rate.

Advantages. The induction stage is rapid and pleasant, and there are rarely nausea and vomiting on recovery. The element of psychic shock is obviated, and patients take pentothal readily for subsequent anaesthetics. The use of narcotics for the relief of pain and restlessness for the first few hours after operation is minimised, and is often unnecessary. Post anaesthetic nursing is reduced to a minimum.

Disadvantages. The use of pentothal for deep

anaesthesia is, in inexperienced hands, not as safe as ether, because the anaesthetist has to depend on a type of respiration characteristic of the drug.

Uses. Pentothal sodium may be employed as a total anaesthtic; for rapid and pleasant induction of anaesthesia preliminary to the use of ether or gas, as a basal narcotic particularly in gas anaesthesia; as a supplement to local or spinal analgesia; in essential hypertension, for estimating the probable value of surgical treatment, as a therapeutic measure for combating the toxic effects of local anaesthetics; for use in convulsive states such as strychnine poisoning, tetanus, and eclampsia; and as a sedative in maniacal states and narcoanalyses.

It is indicated for minor and short operations; operations on the face, head, neck and upper chest; in operations in which the use of the cautery, or diathermy, might lead to ignition of inflammable gases, in orthopaedic operations for the removal of adhesions, of fractures and dislocations, in minor urological procedurs such as cyptoscopy uretral catheterization, lithotrity, passage of sounds, in opthalmic surgery, in minor otorhinolaryngological procedures such as myringotomy and antral puncture, in short dental and oral procedures; in minor neuro

surgical procedures such as lumbar puncture; for nervous and mental patients who fear an anaesthetic mask; as a sedative in maniacal states etc.

Contraindications. It is contraindicated in hepatic disease, advanced pulmonary diseases. in obstruction to the air passages, advanced Diabetes mellitus, starvation and advanced kidney disease. It should not be used for operations on the upper part of the abdomen. Severe cardiac decompensation, coronary disease, myocardial degeneration and low blood pressure are contra indications, as are also severe toxaemia and pyrexia. Obese myxoedematous and extremely ill patients are not good risks.

It should not be used in severe anaemia

Pentothal Sodium as a basal anaesthetic. It can be used as a very transient basal anaesthetic, a use which is even satisfactory for the ambulatory patient, or to produce basal anaesthesia of longer duration, sufficient for example to enable a patient to be transported in the unconscious state from the ward to the operating theatre.

(a) To produce transient basal anaesthesia, a small dose 0.2—0.4 gm is injected as rapidly as possible. The maximum depth of anaesthesia is attained immediately. Then inhalation anaesthesia

or anaesthesia with nitrous oxide can be carried out and spares the patient of the unpleasantness of induction by an inhalation anaesthetic. The dosage employed is so small that it is well below a dose which would be dangerous, that the dose given would usually fail to produce unconsciousness if injected slowly.

(b) If it is necessary to ensure that the effect of the basal anaesthetic will last for 10 – 15 mts a larger dose of the solution (usually about 0.4 – 0.7 gm/ in 10% solution is required) is injected more slowly over a period of obout 60 seconds Injection is continued until the patient just loses consciousness, the dose given being determined by the response. It is better to carry on a matter of-fact conversation with him, stopping the injection as soon as he stops talking.

Signs of anaesthesia with pentothal. During induction, when pentothal is given slowly, yawning and sneezing may occur just before consciousness is lost. If a surgical stimulus is not applied respiration is quite and shallow even during light anaesthesia but during the course of an operation deepning of the respiratory excursion denotes lightening of anaesthesia and is a sign that more pentothal should

be injected. The eye remains still.

(c) Full anaesthesia with pentothal If anaesthesia is to be achieved and then maintained with pentothal alone, the dosage will be such that respiratory depression may be expected and for this reason it is unwise to embark upon anaesthesia unless some form of oxygen under pressure is available, since it may be necessary to inflate the patients lungs. The single dose technique is particularly adapted for manipulative work where maximum anaesthesia and with it maximum muscular relaxation is immediately allowed and where the patient recovers consciousness comparatively quickly, that is usually within about half an hour. The dosage for an average healthy adult is 0.4 –0.7 gm injected as rapidiy as possible.

For short operations premedication is not necessary but where longer operations are contemplated under pentothal anaesthesia alone, the usual morphia and hyoscine premedication is advisable. The morphia assists the pentothal anaesthesia and the hyoscine prevents the secretion of mucus which may otherwise occur from irritation of the mucous membranes by an airway or endotracheal tube.

Maintenance of anaesthesia for longer periods

with pentothal has the disadvantage that it requires another skilled person in order that the airway may be properly supervised throughout.

For operations round the head and neck an endo tracheal tube should be passed so that there is no doubt about the airway being clear.

For maintenance anaesthesia by pentothal a 5% solution is preferred. The needle can be kept in the vein and when anaesthesia shows signs of lightening a further 0.10 gm (i.e. 2 cc of a 5% solution) is injected.

Contraindications.

(1) Children below the age of seven.

(2) Smaller doses for the old or frail persons

(3) Liver disease as in cases of jaundice or intestinal abstructions.

(4) Asthmatic.

Recovery from pentothal. Recovery from 0 3 gm may take 5 minutes from 1 gm an hour and from large doses 3 gm or so recovery may be delayed for 6—10 hours.

(2) Evipal or Evipan Sodium. It is a very patent, drug. It is rapidly decomposed by the liver and so the anaesthetic effect is not so lasting as with pentothal sodium, Recovery takes place rapidly in 20—30 minutes. The dosage and technique are similar to that of pentothal sodium.

CHAPTER XII.

New Antacids.

Aluminium hydroxide. It is an insoluble, colloidal powder which is neutral, amphoteric, and nontoxic. In vitro experiments have shown that it combines with 12 times its volume of decinormal hydrochloric acid within half an hour.

Action. It is demulcent and protective to the gastric mucosa, it is antacid, and it adsorbs toxins It has considerable buffering properties. On contact with the gastric acids aluminium hydroxide forms with them a translucent colloidal gel by the physico-chemical process of adsorption; this adsorptive process effects an immediate rapid decrease in the acidity of the gastric juice, and a more gradual subsequent reduction The p H cannot go beyond neutrality, and the increase is to approximately pH 4. It does not give rise to any secondary production of acid secretion, as do ordinary alkalis such as sodium bicarbonate. The processes of digestion are therefore little affected, and a slight acidity which does not produce erosin; has some antiseptic power.

As a result of some interaction between the aluminium hydroxide and the gastric hydrochloric acid, some aluminium chloride is formed; in the alkaline intestine the latter is again split up with reformation of aluminium of hydroxide and release of the chloride which is reabsorbed. It also has an adsorptive action on the toxins of intestinal putrefaction, on gases, and on bacteria, in the bowel Even with the use of massive doses of aluminium hydroxide. or after prolonged treatment, there is no production of alkaline or other systemic effects such as the production of diarrhoea or constipation, or the formation of intestinal concretions.

In addition to its remarkable antacid properties the colloidal gel formed by aluminium hydroxide in the stomach provides a protective coating to the excoriated or inflamed mucosa, and exerts an astringent action which assists in arresting haemorrhage and healing ulceration.

Dose & method. Aluminium hydroxide can be employed orally in repeated doses of 15 – 50 grains, given before each of the main meals.

Sometimes a suspension of aluminium hydroxide is administered by the nasal drip method

Sometimes a fine tube is passed through the patient's nose and into the stomach, and the antacid is kept running through all night as a constant drip. In this way they buffer and neutralize the acid before it has time to do serious injury to the gastric and duodenal mucosae. The big problem in treating ulcer is to control the acidity at night. During the night all the healing cells which started to grow over the ulcer during the day are digested and destroyed.

Old antacids like sodium bicarbonate and calcium carbonates have certain defects. Sodium bicarbonate is definitely irritating in high concentration and causes a secondary rise of acid. It is systemic in effect and not infrequently causes alkalosis. It releases carbon dioxide thus producing increased intragastric tension. Freely used in large doses for long periods of time it impedes the normal liberation of oxygen by the circulating blood thus causing anoxemia. Calcium carbonate is constipating when large quantities are required for neutralization and releases carbon dioxide Thus the old antacids often caused subclinical alkalosis and perhaps in some alkalemia and toxic manifestations and so the patient

may die of alkalosis.

The use of Aluminium Hydroxide in the treatment of Peptic ulcer.

Collins, Pritchett, Rossmiller. (Journal of American Medical Association Jan. 11, 41) treated 470 cases having active peptic ulcer with colloidal aluminium hydroxide. Of 247 patients who had follow up studies, satisfactory results were obtained in 88%. It has advantages over the usual alkalis aside from its acid—combining power, In addition to its acid combining power, its astringent and demulcent properties are of value. It does not liberate large quantities of carbon dioxide, as do the carbonates; it is not laxative, like the magnesium salts, and its use does not cause a compensatory stimulation of acid secretion like sodium carbonate. It is not absorbed and therefore can be given without the hazards of alkalosis, or precipitation of crystalline phosphates in an alkaline urine. It was given in 246 patients. In certain cases continous drip method of Wuiklestein was used, in others it was given orally during sleeping hours as well as during other hours. During the first week it was given at 12 mid-night and at

2 and 4 a.m. usually in twice the dosage used during the daytime hours. During the second week of treatment. aluminium hydroxide was given at 12 midnight and 3 a.m. The amount used depended on analysis of hourly aspiration of gastric contents during two or more 24 hours periods of management.

Although gastric acidity was not completely and continously neutralized during these periods, aim was to keep the level of free acidity sufficiently low to prevent activation of pepsinogen, the proteolytic neutralization point emphasized by Hollandes. Modification of the Sippy regimen similar to those used by Einsel, Adams and Myers and by Woldman and Palan were used in these cases Liquid petrolatem in 1—2 ounce doses and occasionally magnesium oxide or aromatic fluid extract of cascara sagrada was given at bed time to prevent constipation until the patient was including sufficient vegetable and fruits in his diet to assure proper bowel function.

If the clinical response of the patient was favorable, confirmed by progress roentgen examination and in the case of gastric ulcer, also by gastroscopic examination the use of aluminium hydroxide during sleeping hours was usually discontinued by the end of the second week If it had been given hourly

during waking hours, its administration was then changed to a two hour schedule. and ambulatory managment as mentioned for uncomplicated duodenal ulcer was continued.

Uncomplicated duodenal ulcer. 154 of the patients in this series had uncomplicated duodenal ulcer. Most patients were ambulatory and they carried on with their usual occupation. In most cases the use of 2 drams of aluminium hydroxide every two hours during waking hours for three months proved satisfactory. Either a meal or a glass ful of milk was taken midway between dose of aluminium hydroxide During the next three months a glass ful of milk was taken midway between meals and 2 dram of aluminium hydroxide was taken one hour after each meal, after glass ful of milk and at bed time. During the remainder of the first year's treatment the taking of similar does of aluminium hydroxide after the three main meals and at bed time seemed to prove adequate.

It should be mentioned that certain patients having mild symptoms started treatment with three meals a day and a glass ful of milk midway between meals, taking aluminium hydroxide one hour after each meal, after each glass full of milk and at bed time. In an attempt to maintain a low gastric acidity and owing

to the well known "Ulcer diathesis" of patients having this disease, each patient was instructed to take at least one feeding or a glass full of milk midway between meals for the remainder of his life. If there was a history of seasonal recurrences, the patient was advised to resume the two hour schedule of using aluminium hydroxide two weeks prior to the time of these recurrences each year, usually during the spring and fall, for a period of two months over a five years period of time The healing of any one peptic ulcer does not mean that the patient will not have another ulcer.

Diet.

The diet has become more liberal since the use of aluminium hydroxide has been included as a part of management. The gain in weight of the average patient was as great on this management as was the case in other types of management. Three meals a day, consisting of the usual bland diet, were used at the start of treatment, and within the first week meat has been added. Ground meat was used at the start of treatment in cases of massive hemorrhage. By the end of the second week

vegetables and fruits in cooked form and soon thereafter citrus fruit juice were included. The importance of a well balanced diet has been emphasized in all instances.

Uncomplicated duodenal ulcer 154 cases.

Duration	Continuous remission.	satisfactory results percent
2—11 months (64 cases)	63,	98.4
12—48 months (90 cases)	87.	96.6
average	97.4	%

Complications Duodenal ulcer, massive hemorrhage fifteen patients who had massive hemorrhage from duodenal ulcer at the start of treatment have continued to follow management. Twelve patients or 80 per cent, have obtained satisfactory results. Five patients have been followed for from two to eleven months. and seven have been followed for from one to four years.

Complications. Pyloric obstruction from cicatricial stenosis is a classic indication for surgical treatment. However, the initial roentgen examination may show the presence of pyloric obstruction without actual fibrosis being present. If the condition has been present for a short time, the cause

of the obstruction may be relieved by medical management. These factors were suspected in a group of twenty one cases at the time of the initial examination. 19 patients had relief of the obstruc tion and 12 have been followed, 7 from 2—11 months and 5 for from one to three years.

Gastric ulcer.

37 cases were treated. Satisfactory results were obtained in 33 cases, or 89 per cent.

Magnesium Trisilicate. This synthetic product has an action similar to that of aluminium hydroxide. It is an efficient non toxic antacid which rarely disturbs the motility of the gastro intestinal tract and produces no general side reactions. It does not produce diarrhoea, constipation or alkalosis even in large doses. Dose is ½—1 teaspoonful given one hour after meals.

Tidmarsh and Baxter treated 26 cases with favourable results in 23. 35 grs of magnesium trisilicate was given 6 times a day After 4 8 days the doses were reduced to 4 doses a day. The treatment lasted for four to six weeks

Aluminium Phosphate. Aluminium hydroxide gel in relatively large doses interferes with the absorption of phosphates in man. It may produce

a phosphorus deficiency in the presence of a relative deficiency of pancreatic juice, diarrhea or a low phosphorus diet. It should not produce a phosphorus deficiency in the usual patient with ulcer on the ordinary ulcer diet, which is relatively rich in phosphorus.

Aluminium phosphate gel has antacid, astringent and demulcent properties analogus to those of aluminium hydroxide gel and does not interefere with phosphate absorption. It is as effective as aluminium hydroxide.

Fanley, Freeman. ivy, Atkinson & Wigodsky in Archives of Internal medicine March 1941.

CHAPTER XIII

The Chemotherapy of Tuberculosis

1. Calcium salts. Calcuim salts are of doubtful value in the treatment of tuberculosis.

2. Vitamin D. The vitamin D in the diet has no particular effect on tuberculosis

3. Vltamin A. It also appears not to have any direct action on the tubercular process. Its deficiency in the diet, however causes keratinisation of surface epithelium with a consequent decrease in the secretion of the epithelial glands. This secretion has both a mechanical action in removing and perhaps a direct bactericidal action in killing organisms which may act as secondary invaders in open pulmonary tuberculosis.

4. Copper. Mercader (1934) used a colloidal copper morrhuate with good result.

5. Cadmium in the form of an iodine cadmium sulphide or glycine appears to stimulate the growth of fibrous tissue in animals. In man intramuscular injections of 3 cc of a 1% colloidal cadmium suspension were found by Heaf (1937) to produce results

in 27 cases quite equal to those of gold, with an almost complete absence of toxic reaction. 1% colloidal cadmium sulphide or 1% cadmium sulphide in sterile olive oil was also used. Cadmium is of low toxicity and can be used in patients with high temperatures and toxic symptoms.

K S Ray, N. N. Sen and H. N. Das Gupta report 80 cases of pulmonary tuberculosis treated during a period of 3 years at Jadabpur Tuberculosis Hospital. Fortysix cases were treated with cadmium sulphide alone and 34 cases were treated with cadmium sulphide in combination with phrenic avulsion or artificial pneumothorax.

Technique. A one percent emulsion of cadmium sulphide in sterile olive oil containing 0·25% of phenol was used for injection One c.c.m was given intramuscularly once a week. In some of the afebrile cases with good general condition the same dose was given twice a week The average number of injections given per patieni was 31 8 which corresponds to 0·318 gramme of the sulphide. The maximium number of injections given to a patient was 161 equivalent to 1·61 grammes of the sulphide.

Results of Treatment.

Results were :

(1) Cases benefited with cadmium alone 30·5%

(2) Cases benefited with cadmium and collapse 42·4%.

Out of 80 cases treated with cadium the disease was totally arrested in 16·2 percent and considerably improved in 28·7 percent Out of 59 cases treated with cadmium 37·3 percent became tubercle bacilli negative.

Out of 60 cases cadmium treated 36·6 percent became afebrile.

The results of cadmium therapy are comparable to those of gold therapy. The great advantages are cheapness and freedom from toxicity.

Contra indications of cadmium treatment.

(1) Presence of albumin or sugar in the urine.

(2) Persistent presence of a temperature above 101°F

(3) Presence of diarrhoea, colitis or vomiting.

(4) Presence of heamoptysis.

Reactions and complications do not occur

Gold. Koch discovered that gold prevented the growth of tubercle bacilli in cultures. Sanocrysin, a double thiosulphate of gold and sodium con-

taining 37·4% gold was the first compound used by Mollguard. The action of the compound is not understood., It acts rather by stimulating reticulo-endothelial system.

Toxic reactions. About 50% of cases treated with gold preparations show toxic effects. Sanocrysin is excreted by the kidneys, large bowel, skin and salivary glands and hence toxic effects are most commonly found in these organs. Headache and vomiting sometimes occur immediately after an injection and a rise of temperature is common during the first twenty four hours. Albuminuria is common but is transient. Skin eruptions, exfoliative dermatitis, gastrointestinal disturbances, loss of appetite stomatitis, and diarrhoea are the next commonest. Joint and muscular pains, jaundice, purpura haemorrhagica, agranulocytosis nervous symptoms, mental changes and peripheral neuritis may occur.

Dose. At present a system of graded moderate doses is used. Each case is treated individually, adjusting the dose according to the patients condition and his response to previous injections. Light patients and those with acute disease require smaller initial doses and more careful grading. A usual course is 0·05, 0·1, 0 15, 0·2, 0·3, 0·4, 0·5 gm at

weekly intervals, continuing with 0·5 gm as a maximium dose until a total of 5—6·5 gm has been given. At time of injection the drug is dissolved in sterile, warm distilled water (2cc—5ccm) and given intravenously.

It is better to keep the patient in bed for twenty four hours following an injection, which should be given on an empty stomach. It is better to avoid even slight reactions such as a rise of temperature, by the selection of a small dose When a reaction occurs, no further injection should be given until the symptoms have settled for two days and the next dose should be either the same or decreased if the reaction is severe. Persistent albuminuria necessitates cessation of treatment. The urine should be examined on two occasions before treatment and on the two days following each injection A skin eruption should be considered with great care, as a further injection may precipitate an exfoliative dermatitis.

Reactions are said to be greatly reduced by using 10 ccm of 10% calcium gluconate as the solvent for the sanocrysin. Sanocrysin may alternatively be dissolved in sodium thiosulphate (5 ccm

of 20% solution). Injections of liver extract give even better results in the prevention of accidents. Large doses of vitamins ABC also prevent complications. The cure of skin eruption is often hastened by the intravenous injection of 2 ccm of contramine in 10 cc of 10% glucose.

Other Gold Compounds. The gold compounds can be divided into 3 groups :—

(1) Those soluble in water as sanocrysin.

(2) Those solube in oil as sanocrysrn in oil, Solganal B oleosum. These Compounds are given intramuscularly. These preparations are less rapidly absorbed and less rapidly eliminated: their action is therefore, more prolonged, the reactions following their use are rarer and the ease with which they can be injected is greater.

(3) Those insoluble in oil.

Indications. The patient must be simultaneously under going a sanatorium regime. Most common cases fit for this therapy are :

(1) Recent exudative type. These cases do well with rest alone on a sanatorium regime. If improvement does not take place soon, artificial pneumothorax is the treatment of choice. If the induction is found impossible after three attempts at

different points, then gold is indicated.

(2) Fibrotic type. Artificial pneumothorax is out of question owing to adhesions. Gold may be used in these cases especially if a recent exudative lesion in association with old standing fibrotic disease is present.

Cases must have some resistance as cases with poor resistance do badly on gold.

(3) Collapse therapy and gold. One of the most successful indications for gold therapy is its use in conjunction with collapse therapy. The best results are probably obtained by starting gold as soon as a satisfactory collapse has been obtained.

In old standing fibrotic cases it may be used as a preliminary to operative interference to improve the general condition.

Contraindications. Gold treatment should not be undertaken in the following conditions:—

(1) Old standing cases with much fibrosis.

(2) Very acute cases with marked toxaemia, a temperature above 101° F and cachexia.

(3) Those in the terminal stages.

(4) Patients with gastro-intestinal symptoms-nausea, vomiting or diarrhoea.

(5) Cases with renal disease.

(6) Where any other systemic disease e g. diabetes mellitus is present.

Results. By now, vast number of observers have become disappointed with the drug. In America gold treatment has been largely abandoned. Amberson, Mc mahon and Pesisier (1931) in a very intensive study. using controls who received injections of sterile water, found that there was no evidence that sanocrysin had any beneficial effect, and that in fact, the controls did better. Fishberg (1932) states that "atter a fair trial in various parts of the world, sanocrysin has been abandoned as a therapeutic agent in pthisios therapy by nearly all of its enthusiastic advocates." In France there is a considerable body of opinion against the treatment, some authorities believing that the results do not justify the risk. Urbain Guward (1934) concludes from a study of more than 600 sanatorium patients, that no effect was obtained with the drug. But in England, sanocrysin has had a favourable reception on the whole, and the fact that it is still in considerable use after fifteen years is proof that some benefit has been obtained, Following are the beneficial results of the drug:—

(1) Fall in temperature (where this has been

raised) to normal levels;

(2) Decrease in quantity of sputum with disappearance of tubercle bacilli therefrom;

(3) Moist sounds in the chest clear up;

(4) Radio graphically there is diminution of the shadows due to exudative lesions, and increased fibrosis.

Cases with recent exudative lesions, provided the disease is not too acute or extensive, respond best. Improvement in cases with fibroid disease has also been found but the improvement is usually temporary. Where there is recent exudative disease in association with old fibroid tuberculosis, a favourable result may be expected from gold therapy.

In 1931 Koch studied the reports of 162 investigastors, 62% of whom reported favourable results, 24% found the treatment of no value, while 14% obtained unfavourable results A Japanese Commission in 1927 completed figures for therapeutic results by twenty two European workers, which revealed the following. Improved 51%, unchanged 23% worse 26%. Henrichsen and Sweany (1933) found that on discharge, 63.6% were improved, compared with 24.6% of the controls. Cruden (1933) obtained improvement in 96% of cases with

recent subacute spread of the disease but in only 72% of those with extensive bilateral disease with cavitation. A negative sputum was obtained in 50% of the former, but in 15% of the latter. Pask (1931) found a definite effect on the tubercle bacilli in the sputum in 52% compared with 20% of the controls. Oppen game (1933) noted clearing of the diseased foci on the X-ray in 63% of 43 for advanced cases and a negative sputum in 38.6%. Anson (1934) found X-ray improvement in 67% of his cases, and obtained general improvement in 72%.

Briefly speaking gold is definitely not a cure for tuberculosis. In certain selected cases, some improvement is to be expected in about half the number treated. In a considerable proportion this improvement will be only temporary. Gold therapy has its most successful use as an adjunct to collapse therapy.

Medical press & circular April 24, 1941.

CHAPTER XIV.

Gold Treatment of Rheumatoid Arthritis.

Gold treatment is useful in cases of active atrophic arthritis (rheumatoid or ch. infective) with no obvious renal or hepatic disease

Gold therapy is said to be "the greatest step forward in therapeutics since the disease was first described." It gives results incomparably better than any obtained hither to.

Contraindications Renal or hepatic disease or family history of purpura or other blood abnormality are absolute contraindications for gold therapy.

Gold therapy is effective. It is the most valuable therapeutic measure discovered so far. Pain, swelling and stiffness are relieved but the drug is dangerous and extreme caution is required in its use. It hastens the course of tne disease by producing first an aggravation, then a gradual improvement so that the inactive stage is reached in one year instead of in 20 or 30 years as is often the case without gold.

Parmanil (Bayer is the leat toxic preparation. It

is methyl glucamide of auro-thiodiglycollic acid in a oily solution, containing 50% gold content.

Weekly intramuscular injections were given, beginning with a dose of 25 mg and increasing to 100 mg; total dose for a course was 600 mg given in about 12 injections 50 cases were treated with cures in 4%, marked improvement in 84%, moderate improvement in 6%, slight improvement in 2% and none in 4%, death in none.

These results were compared with those noted in 690 cases treated with older gold salts, in which cure resulted in 10%, marked improvement in 57%, moderate improvement in 13%. slight in 6% none in 11%, death in 3%.

General plan. The plan was to give injection of gold every five to seven days, initial dose was 10 mg, subsequent doses 20, 50 and 100 mg, maximal singal doses 100 mg, total dose for one course 1 gram.

Two to four coursas may be given at intervals of two or three months.

Toxic Reactions. Toxic reactions are common and may prove fatal. They include giddiness, headache, vomiting, abdominal pain, diarrhoea, focal reactions in joints, fever, stomatitis, jaundice. albu-

minuria. various skin reactions from herpes to dermatitis exfoliata, colitis, proctitis, rarely neuritic, and ocular lesions. The most disturbing reaction is exfoliative dermatitis, the most severe is agranulocytosis. Use of the drug should be stopped if the following occur, erythema with slight fever, significant albuminuria, stomatitis, dermatitis, hepatitis or jaundice, purpura, agranulocytosis, aplastic anemia or fall in blood platelets.

Prevention of toxic reactions. One should adhere to the contraindications, examine skin, and urine weekly, make leucocyte and platelet counts, the injections should be stopped at the first sign of any significant reaction however slight. A sudden change from leukocytosis to leucopenia may signify impending dermatitis. The dose should be reduced to 30, 10 or even 5 mg when sedimentation rates approach 10 mm. Severe toxic symptoms may be prevented by giving vitamins. A, B, C, in daily doses of 20,000, 1000, 2,500 international units respectively.

Treatment of Toxic reactions. This is on symptomatic lines. Intravenous injections of sodium. Thiosulphate may be useful.

CHAPTER XV.

Prostigmln.

Prostigmin is a synthetic drug which acts pharmacologically like physiostigmine but has not the untoward effects of the latter drug such as bradycardia, fluctuation in blood pressure depressed respiration, dyspnea and excesstive peristaltic action.

Action. It stimulates the parasympathetic system, and so has marked vagotonic properties. It also inhibits the destructive action of acetylcholine esterase upon acetylcholine, permitting freer transmission of nerve impulses across the myoneural junction and enhancing cholinergic action. It contracts the smooth musculature of the intestine, raises its muscle tone and promotes increasad peristalsis.

In therapeutic doses it causes only a minimal degree of miosis the blood pressure is not reduced and there is no difficulty with respiration. It has no effect on the pregnant uterus.

Uses.

(1) Prevention of Postoperative Distention.

½—1 cc of 1 in 2000 solution is injected subcutaneously some four, six or eight hours or more over a period of the first three post operative days. Better still to administer the drug in 4—6 hourly injections some 18 hours before the operation and continued, if necessary, after the surgical treatment.

(2) Treatment of Post operative distention. The use of prostigimin in the management of post operative distentions and ileus is also successful.

(3) Similarly the use of prostigmin is successful in the prevention and treatment of bladder atony and urinary retentions in surgical cases as haemorrhoidectomy, gynecological laparatomy, hernioplasty etc. Dose is ½—1 cc of 1 in 2000 solution used every 4—6 hours.

(4) It may be used prior to fluoroscopy o X-rays examinations to eliminate shadows due to gas pockets.

(6) In myasthenia Gravis. It is given by intramuscular injection of 2 ccm. Later oral treatment may be instituted one 15 mg tablet given 5 times a day. In mild stages of myasthenia gravis there was complete relief of all clinical signs and symptoms; in more advanced forms relief is less complete but is still sufficient to warrant its use.

(6) In treatment of Peripheral circulatory disturbances. Prostigmin is a peripheral vasodilator and so is useful adjunct in treatment of peripheral circulatory disturbances in which vasospasm is a factor. It was used clinically in 31 cases. 11 cases of thromboangiitis obliterans; 9 of Raynaud's syndrome; 4 of arteriosclerosis; 5 of acrocyanosis, and 2 of acute vascular occlusion. At first each patient was given a subcutaneous injection of 0.5 mg prostigmin. The patients were then given 7.5 mg prostigmin orally three times daily at six hours intervals for a week without other treatment. If no improvement occured, the dose was increased to 15 mg prostigmin three times daily. Of the 11 patients with thrombo-angiitis obliterans treated 7 showed improvement. There was slight improvement in only one of the four patients with arteriosclerosis, in all of whom the degree of vasospasm present was slight, of the nine patients with Raynaud's syndrome, there was marked improvement. Of the five with acrocyonosis, one showed marked improvement and 3 others slight improvement. There was benefit in the 2 cases of acute vascular occlusion.

(7) Prostigmin may be of great help in the elimination of ureteral calculi when antispasmodic

drugs and the usual instrumental interventions have failed.

(8) Glaucoma. Prostigmin is useful in acute and chronic glaucoma. It has a stronger miotic action than eserine but does not cause local irritation and does not deteriorate so quickly as eserine. 5% solution can be used as eyedrops.

(9) It may be mixed with morphine for hypodermic use to potentiate the action of morphia and avoid the drawbacks as habit formation, and acquiring of tolerance. The usual dose of morphia is $\frac{1}{4}$ gr on hypodermic injection but when it is mixed with prostigmin only 8 mg or $\frac{1}{8}$ gr of morphine is required. Prostigmin is used in dose of 1 cc of 1 in 2000 solution. This combination acts much more quickly and all the drawbacks of morphine as constipation, tolerance and addiction are obviated. Morphine used as preoperative sedative and post operative analgesiac caused ileus, distension and anuria in 60%—70% of the cases. When a combination of prostigmin and morphine was used these troubles were got rid off.

CHAPTER XVI.

The New Antisyphilitic Preparations

(1) Sobisminol mass

Scholtz (1939) speak highly of the oral use of sobisminol mass in the treatment of syphilis. It is administered in daily doses representing 0·84 gm of elemental bismuth and is readily absorbed from the gastro intestinal tract. This treatment not only brings about involution of active syphlitic skin lesions but also gives relief in a high percentage of cases of neurosypoilis especially the locomotor ataxia cases. It can be given every day for many months without producing toxic symptoms.

(2) Mapharside. It is a trivalent arsenical compound. It may be produced from arsphenamine by oxidation or converted into arsphenamine by reduction. It has a rapid and beneficial effect upon early syphilis. The drug is much safer than arsphenamine series. Just as with other arsenicals Bismuth, mercury or Iodides may be used concurrently or may follow the course of arsenic.

Dose in 0·02 gm—0·06 gm. It is given intra-

venously. Injection should be completed within 30 seconds once the needle is in the vien

It is said to be much less toxic than arsphena mines.

(3) Massive Arsenotherapy in Syphilis.

Remarkable results in the treatment of primary and early secondary syphilis are claimed by Hayman by neoarsphenanamine dissolved in 5% glucose solution, given by continous intravenous drip, so that 4 grammes of neoarsphenamine were given over five days. The results were rapid healing of lesions and disappearance of treponemas by dark ground illumination within 24 hours; the Wassermann reaction became negative in about 90% of these cases after approximately three months.

CHAPTER XVII.

Use of Bee Venom in the Treatment of Neuritis and Arthritis.

The belief that bee venom was useful in cases of neuritis, muscular pains, sciatica and arthritis was based upon the observation that bee-keepers were seldom found to suffer from the rheumatism. Persons having rheumatism reported that accidental bee stinging brought relief from pain and stiffness in the joints.

B. E. Montgomery treated 22 patients suffering from neuritis and arthritis. Out of these, 11 showed marked improvement, 9 were considerably improved and 2 did not show any improvement.

Technic Injections were made intradermally and as near the seat of pain as possible, but never about the neck or face. A tuberculin syringe and a small 26 or 27 gage short beveled needle were used. The skin was cleaned with ether. The first injection consisted of 0.01 to 0.02 cc. Each succeeding dose, given at two or three days intervals, was increased by 0.01 to 0.02 cc depending

on the reaction obtained until each equivalent to 0.1 cc or one bee sting. When this amount was reached each subsequent dose was increased by 0.1 cc, using multiple injections of 0.1 cc each about ½ in apart. The number of injections was increased at two to three day intervals until a total of 10 bee stings was given at one time or until a secondary reaction was obtained.

The reactions were classified as primary, secondary and generalized.

The primary reaction consists of a broad flat wheel surrounded in a few minutes by a diffuse deep red blush. The secondary reaction consists of a more extensive wheal and considerable edematous swelling accompanied by burning and itching. The generalized reaction is manifested by headache, vertigo, diuresis, diarrhea or generalised urticaria.

CHAPTER XVIII

Drugs For Amoebiasis

Carbarsone. Carbamide-phenylarsonic acid contains about 28·1—28·8 % Arsenic.

It is proposed for the treatment of intestinal amebiasis. It is administered usually by mouth; in acute amebic dysentery or in resistent cases with motile amebas in the stools, retention enemas may be employed. Cutaneous disturbances and other reactions common to arsenic compounds have been observed after its use. The possibility of optic neuritis should also be kept in mind. It is contraindicated in the presence of hepatic and renal damage.

The drug is cumulative and sometimes repeated courses are employed.

Dosage. Orally, for adults, the usual dose is 0·25 gm twice a day for ten days. If necessary this may be repeated following a ten day rest period.

As retention enemas for adults 2 gm of the drug dissolved in 200 cc of warm 2% Soda Bicarb solution may be given after a cleansing alkaline enema every other night for a maximum of 5 doses

if necessary. During this period oral administration is interrupted.

(2) Vioform—iodochlorhydroxy quinoline. Externally it is used as an almost odorless substitute for iodoform, and internally against amebiasis.

Use in Amoediasis. After an initial purge two tablets of enteriovioform (0·25 gramme) are given thrice daily, on a full stomach, for a period of ten days. Clinical symptoms usually disappear after an average of three days and amoebae disappear from the stools after an average of five days.

In severe cases with diarrhoea and tenesmus, enemate made of two or three tablets of enteriovioform in normal saline may be given in addition to the oral treatment.

In chronic cases the treatment may be combined with a course of emetine injections. This combined therapy is much more effective than treatment by either drug alone.

CHAPTER XIX.

The New Antimalarial Drugs.

There are three agents specific in treatment of malaria; quinine, atabrine and plasmochin.

Quinine destroys the trophozoites, schizonts and merozites in all species of malarial parasite but is only slightly destructive to gametocytes, and then only to those of the benign tertion plasmodium, plasmodium vivax and the quartan plasmodium, plasmodium malariae, and is ineffective against the gametocytes of the estivoautumnal plasmodium, plasmodium falciparum.

Atabrine destroys the trophozoites, schizonts, and merozoites of all the species of malaria plasmodia and the gametocytes of plasmodium vivax and plasmodium malariae but has no destructive effect on the gametocytes of plasmodium falciparum.

Plasmachin destroys the trophozoites, schizonts and merozoites of plasmodium vivax and plasmodium malariae but does not destroy those of plasmodium falciparum. Because of this limited action and the

frequent occurrence of toxic symptoms when it is used in curative doses, plasmochin is not used in routine treatment of malaria. This drug is unique in that it is capable of destroying the gameto cytes of all the species of malarial parasites when given in small, non-toxic doses and thus sterilizes man so far as the possibility of transmitting plasmodia to mosquitoes is concerned.

Ataberine tablets are used by mouth. One tablet 0.1 gm is given three times a day for 5 consecutive days. Ataberine masunate is given by intramuscular route dissolved in sterile distilled water.

Quinine Ataberine treatment should be followed by plasmochin treatment in doses of $\frac{1}{8}$ grs for adults two or three times a day or twice weekly until the gametocytes have disappeared.

CHAPTER XX

Mandelic Acid

It is a non-metabolizable substance which when administered by mouth is excreted unchangad in the urine, and if the pH of the urine is kept at 5·5 or less it is rendered bactericidal or bacteriostatic against B. Coli, Aerobactor aerogenes, streptococcus faecalis and organisms of the Proteus, Pseudomonas, Alcaligenes, Salmonella and Shigella groups. The acidity should be controlled by frequent determinations of the pH. In cases in which the acidity is not reduced to pH. 5·5 or less, other acidifying agents such as ammonium chloride, ammonium nitrate or nitrohydrochloric acid may be administered concurrently providing there are no contra indications; the keto genic diet may also be employed. Fluid intake must be restricted to an amount not exceeding 1,200 cc daily. The drug is given for 12—14 days, longer course may cause renal irritation. Nausea, diarrhea, dysuria, and hematuria may also occur occasionally, requiring reduction in dosage or interruption of therapy. It should not be given in the

presence of renal insufficiency, as an inadequate concentration is obtained in the urine; renal irritation may result and serious acidosis may occur from retention of the acid.

Dosage. The usual dosage is 3 gm four times a day.

The best preparation to use is calcium mandalate or mandecal.

CHAPTER XXI.

Serocalcin Treatment in Colds

Serocalcin is a preparation of dried blood plasma. It exerts not only a valuable prophylactic action but possesses in addition an equally valuable curative effects. The preparation is entirely free from side effects.

Prophylactic use. Two tablets are given daily for thirty days. In 2000 cases in His Majesty's Forces this treatment gave 80% good results. These either remained completely immune from colds for a minimum period of four months or else experienced fewer and less severe attacks than usual.

Another group of 431 was given prophylactic treatment with the following results :—

Total percentage of cases benefitted was 83%.

In 62% the protection afforded was four month's.

In 21% the attacks were less frequent and less severe.

In 16% it was a failure,

Treatment. 237 were treated with 2 tablets three times a day.

In 60% of cases colds cleared up in 48-72 hours.

In 29% of cases colds cleared up in shorter time than usual.

In 10% it proved a failure.

yearsley (Medical Press and Circular Oct. 16, 1940)

CHAPTER XXII.

Active Immunization against Tetanus.

The best immunising agent against tetanus is the alum precipitated toxoid. It gives uniformly higher serum anti toxin titers than plain toxoid. The freedom from reactions in the use of alum precipitated toxoid has been universally noted.

The technique is the subcutaneous injection at intervals of 2, or preferably 3, weeks of 1, 2 and 2 c.cm of the toxoid. A final dose of 2 c.cm one year later was recommended to ensure complete and durable immunity.

In the navy the proceedure is as follows:—

i. Two injections of 1. c.cm and 2 c.cm toxoid respectively at an interval of 8 weeks apart to give basic immunisation.

ii. Injection of 2 c cm toxoid at the time of injury if deemed necessary.

iii. Injection of 2 c cm toxoid each four years after basic immunization to maintain immunity at a high level.

The combination of tetanus toxoid with diphtheria

CHAPTER XXIII.

Heparin in Subacute Bacterial Endocarditis.

Subacute Bacterial Endocarditis is due to strepto coccus viridans. So far the disease has proved refractory to treatment. Some success is reported by treatment with sulfapyridine and heparin. Sulfapyridine M & B 693 is given by mouth or injection to combat bacteremia. Heparin is given to increase the clotting time of the blood.

Heparin powder is made up in 350 mg lots and auto claved in 1 litre of normal saline or glucose saline. After a preliminaty injection of 40 mg in 5 ml of saline the heparin is given by continous intravenous drip 15—18 drops per minute running for 9 days in succession. Vitamin c in 200 mg doses is given 4 hrly

(Dockeray, Kaweran, British Medical Journal Nov. 23, 1940)

Heparin has been used with success in the prevention and treatment, of pulmonary embolism in the treatment of phlebitis, in prevention and treatment of thrombosis in various parts of the body.

CHAPTER XXIV.

Treatmest of Pneumococcic Pneumonia with Rabbit Serum.

Undiluted Rabbit serum has surpassed the use of horse serum in pneumonia. It is given intravenously. Before injection, senstivity tests, cutaneous, opthalmic and intravenous are performed.

Reactions. Reactions to rabbit serum are much less. The serious immediate reactions are best prevented by the careful preliminary testing, although the antidote adrenaline should always be ready at hand for immediate use. The onset of a reaction demands immediate cessation of the serum injection. Thermal reactions and the late serum effects occur frequently. They are rarely dangerous and yield rapidly to treatment.

Indications for Rabbit Serum

(1) When the effective sulphonamide derivatives such as sulfapyridine or sulfathiazole are contraindicated.

(2) When the effective sulphonamide derivatives produce no measure of improvement in from

24—36 hours.

(3) When the appearance of various toxic effects of the sulphonamide derivatives develop during administration of these drugs and demand their cessation.

Contraindications. Serum is usually contra-indicated in the patient with a positive conjunctival test. However non-reactor serum can be employed.

Indications for combined serotherapy and chemo-therapy

(1) when the hiscory indicates a 72 hours duration of the disease
(2) when the patient is over 50 years of age
(3) when multiple lobes are involved
(4) when blood cultures are positive
(5) In pneumonia during pregnancy or the puer-perium
(6) when there is serious concomitant complica-ting disease.

Dosage. The dosage of serum usually approxi mates 10),000 units. This is doubled or trebled by such factors as advancing age, bacteremia, increased duration of illness, multiplicity of pulmonary lobe involvement, complicating disease and severity of symptoms. Ordinarily the temperature, pulse

and respiration rate with the general condition of the patient determine the indication for more serum. This should be given at four to twelve hour intervals, until the desired result is obtained.

After the usual test or trial dose is given intravenously the remaining calculated dose is given after one to two hours. The first cubic centimeter should require two minutes while the remainder should be injected at the rate of ½ –1 minute per c·c.

CHAPTER XXV

New Developments In The Treatment of Asthma and other Allergic States.

(1) Adrenalin in Oil. Suspension of adrenalin in pea nut oil—1 c cm of oil containing 2 mgm of adrenalin—is used and is given by subcutaneous or intramuscular injection Dose varies from ½ c.c.—1½ c c. One injection gives relief lasting from 3—24 hours. Adrenalin in oil is slowly absorbed and proves effective in those cases in which injections or inhalations of the aqueous solution have failed

(2) Inhalations ef Adrenalin Chloride. The most effective solution for this purpose is a solution of adrenalin 1 in 100 in normal saline. The solution is sprayed with a good quality hand atomizer with a rubber bulb The greatest benefit occurs when the symptoms are mild or moderately severe. A stronger solution possesses no advantage over this but may give rise to toxic effects such as headache, tremor, palpitation. Duration of inhalation varies 1—4 minutes Long continous use of inhalation

may produce deleterious effects which may be local or general.

Local effects. Some patients complain of tracheal and bronchial irritation and dryness of the throat from too frequent use. Increased cough is noted frequently, immediately after the inhalation. This is due to relaxation of bronchial spasm or shrinkage of bronchial mucosa which releases mucus plugs for expectoration.

General effects. There is general absence of systemic symptoms such as tremor, headache, and palpitation which not uncommonly follow hypodermic injection of epinephrin If 1 in 100 solution produces general toxic effects such as headache a 1 in 200 solution of epinephrin may be used instead.

Ephedrine-barbital-Theophylline in allergy

(3) Brown treated 189 allergic patients (140 with bronchial asthma) He advises capsules containing

Ephedrine sulfate ½ gr
Sodium phenobarbital ½ gr
Theophylline Sodium Acetate 3 gr

This mixture given in a standard gelatine capsule,

was more effective than ephedrine and phenobarbital given alone or combined with other purines. A tablet with an enteric coating that did not dissolve for 3½—5 hours was used for patients whose symptoms began in the early morning.

(4) Aminopylline administered intravenously is effective in intractable acute attacks of bronchial asthma.

(5) Use of Theophyllinc mono—Ethananolamine in Asthma and other Allergies. Theophylline and related drugs have the following pharmacological action: —

(1) It is said to stimulate the psychic areas, and the respiratory, vasomotor and vagus centers.

(2) Increase ease of muscular contraction.

(3) Lead to vasodilation by a direct action on the vessels (this combines with the cardiac stimulation to quicken the circulation) and lead to diuresis from the interaction of several factors.

(4) Lamson and Bacon treated 153 patients of asthma and other allergic states. All these patients were rather of severe type who were not benefited by the usual drugs. To start with minimum doses of the drug (theamin, Lilly) were used. A one grain capsule was taken to anticipate and prevent

or abort symptoms. If in from 20—45 minutes the desired result was not obtained the dose was repeated and titration continued to a maximum of six capsules. If maximum doses by mouth failed to give relief a solution of 25 mg per cubic centimeter was used intravenously in doses of 2 to 5 cc. This brought prompt relief in every instance.

77—88 per cent patients obtained relief from no more than 4 grains. Untoward effects were inconspicuous. Vasomotor rhinitis paroxysmal dyspnea, generalised eczema, urticaria and angioneurotic edema were also benefitted by this treatment.

CHAPTER XXVI.

New Antiscabietics

(I) Colloidal Sulfur Treatment in Scabies

George V. Kulchar and Willard. M. Meininger advocate the treatment of scabies by the precipitation of colloidal sulfur on the skin through the interaction of sodium thiosulfate and an acid. The method is :—

Treatment.—After the patient has taken a soap and water bath and is thoroughly dry, a 40 percent aqueous solution of sodium thiosulfate is applied over the entire body with the exception of the head and face. Special attention should be directed to the areas between the fingers, flexural surfaces of the wrists, breasts, abdomen, buttocks, thighs and external genitalia. Fifteen minutes later, 4 percent hydrochloric acid is similarly applied, and one hour later the applications are repeated in the same order. The procedure is repeated the next day; on the following day the patient again bathes and puts on fresh clothing. All bed linen, sleeping garments and clothing previously used are sterilized

by boiling for five minutes.

(2) The Derris Root Treatment of Scabies Derris or tuba root consists of the dried rhizome and roots of the Derris elliptica Benth and Derris Malacensis Prain, climbing plants that are cultivated in the Federated Malay states, Sarawak, Singapore, Sumatra, and Johore. The powder has a slight odour and a bitter taste, and on inhalation produces a feeling of numbness in the tongue and throat. The root contains a crystalline substance called rotenone. It may be present upto 10%. The active constituents are soluble in acetone, benzene, chloroform, ether, and carbon tetrachloride. They are insoluble in water, weak acids and alkalis. Derris is used in agriculture as an insecticide especially against the warblefly.

Leslie Saunders. (British Medical Journal 26-4-41)

Used a lotion of derris root powder for scabies. 4 ounces of derris root powder is added to 1 gallon of water and stirred and 1 oz of soft soap or powdered soap or soap flakes are added. This lotion is rubbed all over the body with cotton wool and allowed to dry Particular attention is paid to the spots on the hands, wrists, armpits and groins. The

application was made twice a day morning and at night. Baths before or after the treatment are not necessary. Patients are cured in from 6-14 applications. The treatment is of great value where water is scarce and baths are difficult to procure. It dispenses with the trouble of having clothes disinfected. The bed clothes or under clothes are not stained.

The disadvantage of the method is that some patients complain of a burning sensation in the region of the scrotum and penis after 4-5 applications. There may be a mild excoriation in these sensitive regions. This defect is overcome by the use of weaker lotion for these parts.

Benzyl Benzoate Treatment of Scabies

(3) The lotion for the treatment of scabies consists of equal parts of Benzyl Benzoate, methylated spirit and soft soap B. P. One case requires 1½ oz of this lotion.

Method—Anoint the body with soft soap, rubbing it with special care into those parts commonly attacked by the acarus (i, e, the groins, inner aspects of thighs, abdomen, axiliae, wrist and between the fingers). Then soak for 10 minutes in a bath at

100° F, the patient rubbing the affected areas thoroughly during this time. While the body is still wet apply the lotion vigorously for five minutes by means of a pig hair bristle shaving brush. This must be done very thoroughly and all parts must receive attention, particular care being paid to the infected areas. Allow the lotion, and the leather produced to dry on the skin and again apply the lotion vigorously for a further five minutes. Then dry the body with a towel

The patient now resumes the clothes worn before treatment. 24 hours later a bath is taken and clean clothes are put on. The discarded underclothing and the bed cloths used by the patient should be sterilised by boiling It is important that the close contacts of the patient should be treated on the same day, even though they show no signs o the disease.

(British Medical Journal,
Nov. 9, 1940.)

CHAPTER XXVII.

The New Sympathomimetic Drugs.

(1) Ephedrine

(2) Benzedrine

Ephederine.

It produces effects somewhat similar to those of adrenaline. It has a direct stimulant action on the smooth muscle as well as a stimulating effect on the sympathetic nervous system. In small doses it has a stimulating action upon the heart, increasing the rate and the strength of contractions and raising the blood pressure. It raises the blood pressure mainly due to vasoconstriction. Other effects similar to those of adrenaline are dilatation of the bronchi and mydriasis after local or systemic administration. On local application to mucous membranes or wounds it contracts the capillaries to a moderate degree and thus diminishes hyperemia and reduces swelling. Ephedrine is used locally in the eye to dilate the pupils and in the nostrils to shrink the congested mucosa in rhinitis and sinusitis. The systemic effects

can be obtained by oral as well as by hypodermic or intramuscular administration. It is useful in asthma hay fever and urticaria. It tends to produce symptoms of the anxiety complex. It is contraindicated in serious heart disease.

Dose.

1 As a spray $\frac{1}{2}\%$—2%

2 In opthalmologic work 4% solution locally.

3 Oral $\frac{1}{3}$—$\frac{1}{6}$ gr every 3—4 hours.

Ephederine in myasthenia Gravis. Ephedrine is definitely beneficial. The best drug being prostigmin and a combination of ephederine and prostigmin may be used.

Ephederine in Nocturnal Enuresis. Given before retiring to bed ephedrine influences the depth of sleep so that normal pressure of urine in the bladder suffices to waken the patient; the most refractory cases responded to this treatment. (S. Muntoner)

Benzedrine.

Amphetamine (Benzedrine) Sulfate is a sympathomimetic drug. It causes relaxation of the smooth muscle of the viscera and constriction of the smooth muscle of the arterioles with a rise in blood pressure lasting for 1 –2 hours. It dilates the pupils, widens

the palpebral fissure, increases intraocular tension and decreases power of accomodation, thus resembling atropine. It relaxes the gut musculature and reduces peristalsis. It has sympathetic effect on the cardiac muscle. Ocular effects are produced by instilling 0·5 to 2 per cent of the solution. It has no pronounced effect on the cardiac muscle.

It produces a sense of wakefulness increased vigour and pleasure and a feeling of increased physical and mental power. These are due to central action.

Uses. (1) As vaso constrictor in rhinitis or vasomotor rhinits sinusitis, hay fever and asthma by inhalation, or local application by means of a spray or dropper, of a 1% solution in liquid paraffin.

(2) Paroxysmal Hiccup. Benzedrine Sulfate inhalations are effective in controlling the paroxysmal contracting of the diaphragm.

(3) It is useful in the treatment of chronic alcoholism. Two or three 10 mg tablets are given daily by mouth There is no habit formation, patients feel alert and energetic and no longer feel the need to drink. Individual drops the drug after the desired results of prolonged abstinence from alcohal had been reached

(4) It is useful in narcolepsy, post-encephalitic Parkinsonism, intestinal spasm. It gives favourable results in orthostatic hypotension but is inferior to ephedrine

Contraindications. (1) It should not be permitted to be used to overcome simple physiologic fatigue, and to enable the individual to carry on a few more hours. It is contraindicated in individuals with idiosyncratic reactions, in cases in which sleepness is a prominent symptom, except when combined with sedatives, in hypertension, and cardiac diseases and in marked atony of the gastro intestinal or gastro-urinary tract.

(5) Benzedrine is the drug of choice for obesity. Obese patients with habit of over eating are the best subjects. A diet of 1200—1500 calories is given daily. The fluid intake is restricted and regular bowel motion is made certain. For three weeks the drug is given regularly and is stopped in the last week of every month. Weight should be lost about 15—20 lbs a month. The dose of the drug is the smallest effective dose in the begining which is increased gradually.

CHAPTER XXVIII.

Miscellaneous Therapeutic Agents

(1) Veratrum Viride in Treatment of Eclampsia

Richard. D. Bryant and John. G. Fleming reported a series of 120 cases of eclampsia treated with Veratrum Viride. There were only two deaths in the entire series, a mortality rate of 1·67%.

The effect of a hypodermic injection of a therapeutic dose of Veratrum Viride is startling and may cause undue alarm to those unfamiliar with the effects. The blood pressure falls rapidly sometimes to as low as 50 systolic. This marked fall is transitory, but is followed by a more or less prolonged period during which the pressure is well below the original level. The heart beat is slowed to 40 per minute in some cases, but it soon picks up and remains at 60 to 80 untill the effect of the drug wears off. It causes copious vomiting and the respiration is always slowed considerably. The individual susceptibility to the drug is marked and therefore the size and number of the doses can be geuged only by the reaction of the patient.

Aminophylline in the Treatment of Angina Pectoris

Theobromine and theopylline and other members of the series are potent vasodilators of the coronary arteries.

Aminophylline. Dose is 0·2 gm three times a day. If no effects are produced it may be increased to 0·8 or 1 gm. Aminophylline benefitted 75% cases of angina pectoris.

The drug may be used for weeks and months without any untoward effects.

(Journal of American Medical Association March 8, 1941)

Use of Quinine for Relief of "Night Cramps" in the Extremitis

Painful tonic spasms of muscles in the extremities of middle aged and elderly patients with little evidence of serious structural changes of the pripheral blood vessels are difficult to treat.

Harold. K. Moss and Louis G. Hermann report results with quinine in 15 cases. Beneficial effects were noted in all· Sometimes the effects are permanent.

One 3 or 6 grs of quinine sulfate tablet is given

in the morning and one at bed time.

Use of Adrenalin in Dysmenorrhea

The Vagii cause constriction of the utrine muscle and so cause menstrual cramps. Hypodermic injection of adrenalin stimulates the sympathetics which relax the uterine musculature and thus relieves the pain of dysmenorrhea which is caused by muscle spasm produced by over activity of impulses through the vagii. Wolf treated seven patients with dysmenorrhea by hypodermic use of adrenalin. Five patients got immediate relief

Beta-Phenylalkylamine in Prevention of Nocturnal Enuresis

S. Muntner advises the use of the above drug some two hours before going to bed. The dose for children up to the age of 10 years in 3 mg for adults it is 6 mg. It may be regarded as a specific for symptomatic treatment.

The second best drug for this trouble is ephedrine given in the usual doses.

Syntropan, for Evacuation of Ureteral Calculi

Syntropan is a synthetic derivative of atropine which acts on the parasympathetic nerve endings

and also on the smooth muscle fibers. It is principally spasmolytic. Its action on the muscle tonus is more selective than that of atropine, and it act much less on the vascular system and on the glandular secretion; therefore much higher doses than those of atropine can be given safely and for a longer period. One to two tablets or even three or four may be given daily. In the presence of strong ureteral spasm or when a colic can not be stopped by catheterization syntropan is given intravenously in daily doses of ·01 to 0·03 gm (Hans Wildbolz)

Acetylcholine in Treatment of Arthrosis, Deforming Arthritis and Muscular Hardness and to Revive Paralysed Muscles

Acetylcholine is a parasympathetic drug, and causes overfilling of the blood vessels of the extremities. It relieves pain, improves mobility and stimulates muscular activity in deforming arthritis. It causes increased blood flow in the paralyzed muscles but disagreeable general symptoms have never been observed. Dose is 0·1 gm in 2 cc of sterile water given intramuscularly. (E. Peyer)

Histamine in Night Sweats of Phthisis

F. Costs. M. Lamottee, and G. Gmot have used

daily dermal injections of histamine bihydrochloride to combat the night sweats of tuberculosis. They start with a dose of 0·1 mg and increased daily by 0·1 mg till 1 mg is reached, the total dose given being 5·5 mg 15 fifteen patients were treated with good results.

Trasentin

Trasentin diminishes or abolishes spasm and contraction of stomach and intestines produced by various drugs or by vagal stimulation. Small doses of trasentin had a definitely relaxing effect on the gall bladder and counteracted the effect of pilocarpine on the urinary bladder. Their relaxing effect on smooth musculature is due to two factors, one of which acts directly on the muscle and one on the parasympathetic nervous system.

Papillomata and Verrucae treatment with magnesium chloride.

Intravenous injection of a 20—40 % solution of magnesium chloride is given daily or on alternate days, commencing with a dose of 0.05 grammes and increasing this by 0·05 grames on each occasion up to a maximum dose of 2.0 grammes

with slight variations according to the age and condition of the patient (Gillies Anan, Medical Press & Circular August 2, 39)

Treatment of Acne Vulgaris with Insuline.

Acne Vulgaris is regarded as aetiologically related to the endocrine system. Its first appearance at puberty and its frequent aggravation just before or during the menses, strongly support that view. Hyperglycaemia was reported in 5 1% of their cases of acne by Lewis and Kahn. Injections of protamine zinc insulin in 5—10 units twice a day for a few weeks have proved useful.

Potassium Chloride in Familial Periodic Paralysis.

It has been found that the attacks of paralysis in this disease are associated with a fall in the serum potassium, and the administration of potassium salts brings about rapid recovery in the power of the muscles.

Potassium Chloride—5—10 grams – dissolved in water given by mouth, will bring about recovery in half to two hours. If given intravenously the effect is much more rapid, but the patients complain of severe pain along the course of the vein.

Morphine-Scopolamine Anasthesia; First Aid Treatment of the Injured.

It may be used in the first aid room, for persons requiring an anesthetic for treatment of fractures, dislocations, wounds requiring special care and burns.

The usual initial injection consists of $\frac{1}{4}$gr morphine sulfate and $\frac{1}{50}$ gr scopolamine hydrobromide. For only the extremely young or aged is the dose smaller; it is usually decreased to $\frac{1}{6}$ gr morphine and $\frac{1}{100}$ gr scopolamine. If, as in the case of fracture requiring much manipulation, a deeper and more prolonged anesthesia is desired a second and third dose of morphinescopolamine is given, the size depending on the condition, age, sex and weight of the patient.

Most men between the ages of 18 and 60, weighing 150—200 lbs, will require two injections of $\frac{1}{4}$ gr morphine and $\frac{1}{50}$ gr scopolamine and a third injection of $\frac{1}{6}$ gr and $\frac{1}{100}$ gr respectively. Most women from 18—60 and weighing 120—150 lb. require one injection of $\frac{1}{4}$ gr morphine and $\frac{1}{50}$ gr scopolamine and two injections of $\frac{1}{6}$ gr and $\frac{1}{100}$ gr respectively. Injections are given 30—40 minutes apart, and the patient is observed constantly, espe-

cially with regard to pulse rate and respiratory rate. If the respiratory rate reaches 10—12 per minute, no additional injections are given.

Value of Banana and Banana Powder in Treatment of Infants and Children having Diarrhea.

Irving J. Wolman and Rudolph L. Roddy (Univ. of Pennsylvania) report a two year investigation of the use of banana powder in the treatment of hospitalized infants and children having diarrhea.

97 infants and children were given mashed banana powder as the principal food. Infants under 6 months of age were fed banana powder in watery solution. Older patients received ripe bananas freshly mashed. There were no differences in the effects of fresh ripe banana as compared with those of banana in the preserved powdered form.

For the first 48 hours, the infants received (1) mashed ripe banana, $\frac{1}{3}$ of a banana ($1\frac{1}{6}$ oz) per lb. body weight per 24 hours, or (2) 1 table spoon banana powder per pound body weight per 24 hours as a paste or as a 7·5% solution in water or in half strength pysiologic solution of sodium chloride. These were offered every 2 hours during the 12 hours of the day and every 4 hours during the night.

For the second 48 hours, infants under 2 years were given (1) well boiled skimimed milk, 1½ oz per lb body weight per 24 hours, with powdered banana added up to 7·5% of the formula, equal feeding spaced at regular hours, and (2) boiled water liberally between feedings.

Older children were given cereal cooked with water, toast, potatoe, rice or barley gruels etc.

After 96 hours the full regular diet was begun. If the diarrhoea recurred, the bannana regimen was renistituted.

Pectin Agar for Diarrhea in Infants and the Newborn

Pectin agar is composed of 6·3%, pectin 4·3% agar and 89·4% dextrimaltose. One cup or 8 oz by volume of the powder is equal to 480 calories.

In preparing a formula for nurslings 1 cup of the powder is cooked 10 minutes with 24 oz milk. While still hot the desired amount is poured into nursing bottles. After re-warming and shaking the preparation feeds easily through a nipple with an enlarged opening. The treatment of diarrhea at any age consists of limiting all intake to the pectin-agar formula and water until the stools are formed.

An increasing number of clinicians deem it rational to give a high carbohydrate diet to infants with acute gastro-intestinal disturbances, particularly if associated with parenteral infections The pectin-agar-dextrinmaltose preparation fulfils this requirement and thereby tends to combat ketosis and vomiting The pectin acts as a detoxicant, adsorbent and healing agent, and the preparation is in a vehicle which promptly controls the diarrhea.

Titanium in Skin Diseases

Titanium is nontoxic. It has proved very useful in many skin diseases. In eczema, after the diminution of exudation their use brings about regression of the erythema and pruritus and a rapid regeneration of the epithelium. It may be used in the form of an ointment of Titanium Salicylate, Titanium Peroxide, Titanium oxide or Titanium Tannate. in 2—5% strength.

It proved useful in pruritus ani after all other measureshave failed. In Sycosis Barbae, the response was prompt. In Keloid, application of the ointment morning and evening over a period of 3—5 months led to gradual disappearance of the keloid.

(J. Metadier, the Medical Press & Circular
December 27, 1939)

A New Method of Treating Leucoderma

The leucoderma patch is carefully cleansed with alcohol, and the oil of Babchi seeds (Psoralia Corylifolia) is injected intradermally using an ordinary hypodermic syringe fitted with a fine needle. The amount of oil in each individual injection is a single drop. The number of injections varies with the size of the patch, small spots of 1 ccm or so in diameter requiring a single injection in the centre. In larger patches the injections are spread about 1 cm or a little more apart, until the whole area is covered. In two to three weeks, formation of pigment can be noticed, begining at the site of the puncture from which point it spreads centrifugally.

If, when deposition of pigment ceases, the contiguous areas of pigmentation have failed to coalesce, a second or a third course of injections can be given in the intermediate white patches, until the whole area is normally pigmented.

The injections are followed by a good deal of pain.

(Panja, Maplestone, Indian Medical Gazette Feb. 1940)

Stimulants

Coramine, and cardiazol are now used in the attempt to restore failing respiration and circulation, especially in severe infections, after anaesthetics, and in cases of over dosage of hypnotics. Formerly only strychnine, caffeine, and solutions of camphor and ether in oil were used to any extent, but they were not very satitfactory. The names coramine and cardiazol are misleading as they suggest that their chief action is on the heart; this is not the case. Their action is similar to that of picrotoxin. The chief effect is on the brain and medulla and they are essentially stimulants of the central nervous system, tending to restore consciousness and to augment respiration and blood pressure by their action on the medulla. Their action is analeptic ("awakening"). As stimulants to accelarate recovery from anaesthetics and to augment breathing, picrotoxin, coramine cardiazol and strychnine are equally effective.

As antidates to poisoning by barbiturates picrotoxin, and cardiazol are far superior to the other analeptics; indeed there is some evidence that coramine and benzedrine may be actually harmful.

There are other drugs the action of which on

the circulation is mainly peripheral, that is on the heart and blood vessels. Their action simulates, to a greater or lesser extent, that of adrenaline. Of these drugs the best known is ephedrine the use of which in restoring the circulation, by combating the fall of blood pressure which may occur in spinal anaesthesia, is well established. It has got some central action as well.

Benzedrine has a characteristic stimulant action on the higher psychic centers; it leads to increased self-confidence, lessened fatigue, good humour, talkativeness and sleeplessness. It is of paramount value in treatment of narcolepsy.

Lobeline stimulates specially the respiratory center by lowering the thresh hold of its response to carbondioxide. Lobeline and carbondioxide are used in the treatment of asphyxia of the newborn, carbon monoxide poisoning and respiratory arrest during anesthesia. Lobeline is contraindicated in myocardiol disease as it depresses the heart.

Drugs Acting on Plain Muscle.

The most widely used for its action in causing contraction of plain muscle is pitiutary posterior lobe extract.

Its two constituents have been separated:—

(1) Oxytocic or uterus contracting principle

(2) Pressor or arteriole contracting principle with it is possibly associated or identical is the substance causing contraction of the muscle of the gut as well as the antiduiretic principle. This is used for combating distension of the abdomen by improving gut tonus and aiding peristalsis. The action is directly on the muscle.

(3) Intestinal tonus and peristalsis may be augmented also by drugs which affect the vagal neuromuscular mechanism. Acetyl choline transmits the nervous impulse from the vagus to the intestinal musculature. When injected it causes increased peristalsis but in practice a substance Doryl is used which is allied to it.

Physostigimine was formerly used for stimulating peristalsis. It acts by preventing the destruction of the naturally formed acetylcholine in the tissues. But now a better product prepared synthetically, called prostigmin is used for same purpose.

If prostigmin is combined with the ext. of posterior pituitary or pitressin the action is synergised and the effect is greater, doryl and prostigmin causes contracion of the muscles of urinary bladder as well

and are used in postoperative distention of the bladder

Drugs causing relaxation of the tonus of the plain muscle.

In certain forms of colic, e.g. biliary, renal and intestinal colic problem of relaxing spasm of plain muscle arises. This is achieved by inhalation of amyl nitrite but the effects are transitary though rapid. Better still that tablet of nitroglycerine be chewed

For prolonged effects papaverine, one of the alkaloids may be used. In contrast to morphine it causes relaxation of plain muscle. Eupaverin is a synthetic drug with similar action. Atropine which paralyses or diminishes the vagal nerve mechanism which is motor to the organs, or drugs allied in action to adrenaline which simulate the inhibitory effect of the sympathetic nerve supply also cause relaxation of plain muscle of the intestinal, biliary and renal tracts.

Phenothiazine - a new anthelmintic.

Phenothiazine is a fine, smooth, pale yellow powder insoluble in water, is effective against intestinal worms in sheep and dogs. It is excreted in the urine and acts as a urinary antiseptic. Domestic animals are remarkably tolerant to the drug and there

is a wide margin between the therapeutic dose and toxic dose. Even 80 times the effective anthelmintic dose without any signs of intoxication has been given. Repeated small doses are, however. considerably more toxic than occasional large one.

P. Manson Bahr (Lancet December 28, 1940) tried it as an anthelmintic in man.

It was found to be very useful in round worm and threadworm infections but useless in hookworms. In Roundworm Infection 8 gm of drug in powder form given on three consecutive mornings followed by 3 drams of sodium sulphate gives good results.

Threadworms. Children under 8 years. A dose of 2 gms daily for 7 days is sufficient, for children under 4 years half this quantity is required.

Adults. 4—8 gms daily are given for 7—10 days. The drug is tasteless.

Use of Antiseptic Snuffs in infections of the upper respiratory tract.

Several snuffs were tried for their antiseptic action in the nose the best ones are:—

(1)	R	Pencillin	1 part
		Menthol	5 parts
		Lycopodium	94 parts
(2)	R	Sulfathiazole	10 parts

Magnesium carbonate 90 parts.

These snuffs are of use as a prophylactic against bacterial infection of the upper respiratory tract and may prove effective in the prevention of cerebros pinal meningitis as the channel of infection is always the nose and may cure nasal carriers. But it is not effective in the prevention and treatment of the common cold.

(The British Medical Journal, Feb. 1, 1941)

Intranasal immunization against

Diphtheria, Tetanus, Streptococcal and Staphylococcal. Infections, and Whooping cough.

Ramon, Zoeller and Jensen immunized a number of children with diphtheria toxoid by the intranasal route. A small pledget of absorbent cotton wool soaked in 0·5 ccm of toxoid and inserting it through the anterior nares till it rested between the septum and anterior end of the inferior turbinate bone.

The pledget remained in the nose from 15 mts to 6 hours. 83% of the entire group showed a good response. Glycerine cabolic saline solution of the toxoids of diphtheria, tetanus, streptococcii, staphylococcii may be used. If multiple immuniza-

tion is required a mixture of any two or all the toxoids may be used.

(The British Medical Journal Jan 4, 1941)

Zipp in the treatment of wounds

Zipp is	Zinc oxide	1 part
	Iodoform	2 parts
	Liquid Paraffin	2—3 parts

Mixed to the consistency of clotted cream. It is a modification of b i.p.p., with it there appears to be no risk of iodoform poisoning. It stimulates healing and has a beneficial systemic influence, It may be used for plaster method of treating wounds. Its indications are same as for bipp

(Lancet 30, November, 1940)

Strontium Bromide in Asthma

G. S. King used (15 grs per 10 cc) strontium bromide intravenously in cases of asthma. Immediate relief was experienced by patients who had become tolerant to adrenaline, ephederine, barbiturates and opium derivatives, and no untoward results were experienced when the drug was administered slowly A diffused feeling of warmth or heat is experienced if the drug is not injected slowly, and the immediate

relief is never accompanied by a feeling of discomfiture, palpitation or tachycardia. The sedative effect of the bromide is much more prolonged than with other drugs. When relief is not immediate, a second or third injection may be given without reference to time, since the drug is non-toxic. No analphylactic reactions were noted and even in patients sensitive to bromides only local or skin manifestations were evident. This therapy is of particular value in cardiac asthma or in asthmatics who are neurotic or who have marked arterio sclerois and hypertension. Strontium bromide is non toxic and non-cumulative and exerts a direct sedative effect on the nervous and reflex system.

Rhubarb in the treatment of Acute Bacillary Dysentery

The most effective and easiest treatment for bacillary dysentery is with rhubarb. One teaspoonful of powdered. Turkey rhubarb root is given every hour. The treatment is stopped when bile appears in the stools.

Treatment of Carriers of Typhoid, Paratyphoid infections

The only drug which was found effective for the carriers of typhoid-paratyphoid group is Soluble

Iodophthalein. All other drugs are useless. The drug is given orally in doses of 4 gm in the form used for X-rays examination. It is repeated twice in the next six day.

The use of Cassia Fistula in the Treatment of Black-Water Fever.

1000 grammes of the powdered root-bark was exhausted with cold 60% alcohol by the reserved percolate process 800 c c m of the percolate was obtained thereby to which was then added 100 c.cm of glycerine and the final volume was made up to one litre with 60% alcohol. The extract was filtered after keeping for a fortnight This extract was given to cases of black-water fever in doses of ½—1 drachm repeated every four hours. The urine cleared invariably in 3—4 days after the administration of total quantity of 12—16 fldrachms. The percentage of cures worked out at 96·3

Venkatachalam and A. N. Ratnagiriswaran,
(The Indian Medical Gazette
April, 1941)

ERRATA.

Page.	*Line.*	*Correct.*	*Mistake.*
16	21	90	0,9
21	5	strength	streugth
24	1	about proper healing	obout prop rhealing
29	16	greatest	geatest
32	19	serious	serions
32	21	or	ar
32	22	pregnancy	pregnancn
37	17	deficiencies	eficiencies
44	20	50,000 units	5 000 units
46	19	inertia	nertia
47	2	give in	given
47	9	5 mgm	5 mgn
67	14	insulin	inuline
72	19	susceptibility	suspectibelity
88	9	pint	piut
95	12	immobilisation	immobilisafion
107	15	and	end
114	5	showed	should
118	12	well	will
118	20	1 in 300	1 m 300

Page.	*Line.*	*Correct.*	*Mistake.*
118	21	1 in 5	1 m 5
134	21	cystoscopy	cyptoscopy
139	2	potent	patent
148	19	4—8 days	4 8 days
151	20	31·8	318
161	20	courses	coursas
169	17	0·01—0·02	001—002
171	7	employed	employed
187	9	expectoration	oxpectoration
200	16	is	in
209	7	satisfactory	satitfactory
209	20	antidotes	antidates

INDEX.

—

REFERENCES.

Annals of Internal Medicine		March 41
Bethea Year Book of General Therapeutics		1940
British Encyclopaedia of Medicine		
Bicknell F. The Medical Press and Circular		28 2-40
Cruickshank J. N.	The Practitioner	May 1940
Coplans. M	M P. & C.	6-9-39
Cyril. R. B.	M. P. & C.	5-741
Davidson. S.	B. M. J.	7-10-39
Dryerre. W. H.	B. M. J.	13-5-39
Dockerary. C. J.	B. M. J.	23-11-40
Fantus	Y. B. G. T.	1936
Folch A.	B. M. J.	20-4-40
Haultain W. F. T.	B. M. J.	25-5-40
Hench. P. S.	Annals of Internal Medicine	March 41
Harcourt. J. D.	B. M. J.	20-4-40
Health Bulletin	No. 32	1938
Horace Hill	M P. & C.	12-7-41
Horsley. J. S.	M. P. & C.	24-1-40
Kawerau. E.	B. M. J.	23-11-40
Lawrence. R. D.	B. M. J.	27-5-39
Macpherson. A.I.S.	B. M. J.	25-5-40

Mc Callum. E.	B. M. J.	25-5-40
Medical Clinics of North America		January 1941
Moore. H.	The Practitioner	Oct. 1940
Murless. C. B.	M. P. & C.	6-9-39
Minski. L.	M. P & C.	27-3-40
		20-3-40
		25-12-40
Metadier. J.	M. P. & C.	27-12-40
Nevin. S.	M P. & C.	28-8-40
New & Non Official Remedies		
Practitioner		Feb. 1940
Part. B. F.	M P. & C.	11-12-40
Purandare	Medical Bulletin	4-1-41
Sutherland D J.	B. M. J.	7-10-39
Sutherland. R.	M. P. & C.	24-4-40
Shah. K. A.	Medical Bulletin	1-3-41
		15-3-41
Sovani. V. S.	,, ,,	18-1-41
Shafer. J.	M. P. & C.	13-12-39
Stevens. J. M. M.	M. P. & C.	17-7-40
Winterton. W. R.	M. P. & C.	6-9-39
Williams. L	M. P. & C.	6-12-36